

**UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS**

CARYL HULL LEAVITT, Individually and on behalf
of all those similarly situated,

Plaintiff,

v.

ALNYLAM, INC., JOHN M. MARAGANORE,
MANMEET S. SONI, YVONNE L.
GREENSTREET, AKSHAY K. VAISHNAW, and
BARRY GREENE,

Defendants.

No. 1:18-CV-12433-NMG

JURY TRIAL DEMANDED

AMENDED CLASS ACTION COMPLAINT

Lead Plaintiff Tunc Toker (“Plaintiff”), individually and on behalf of all other persons similarly situated, by Plaintiff’s undersigned counsel, brings this securities class action under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 (the “Exchange Act”), and Rule 10b-5 promulgated thereunder, on behalf of himself and all other persons or entities who purchased or otherwise acquired the securities of Defendant Alnylam Inc. (“Alnylam” or the “Company”) during the period from September 20, 2017 through September 12, 2018, both dates inclusive (the “Class Period”), and were damaged thereby.

Plaintiff alleges the following upon information and belief, except as to those allegations concerning Plaintiff, which Plaintiff alleges upon personal knowledge. Plaintiff’s information and belief are based upon Lead Counsel’s investigation, which included a review and analysis of, *inter alia*: (i) regulatory filings made by Alnylam with the United States Securities and Exchange Commission (“SEC”); (ii) a review and analysis of Alnylam’s conference calls including conference calls on which the Individual Defendants¹ participated; (iii) wire and press releases; (iv) reports; (v) filings with the U.S. Food and Drug Administration (“FDA”); (vi) analyst reports and advisories about the Company; and (vii) information readily obtainable on the Internet. Plaintiff believes that additional substantial evidentiary support will exist for the allegations set forth herein after a reasonable opportunity for discovery.

¹ The Individual Defendants, defined in further detail below, are Alnylam’s Chief Executive Officer (“CEO”) John Maraganore (“Maraganore”); Chief Financial Officer (“CFO”) Manmeet Soni (“Soni”); Chief Operating Officer (COO) Yvonne Greenstreet (“Greenstreet”); President of Research and Development Akshay Vaishnaw (“Vaishnaw”); and President Barry Greene (“Greene”). Alnylam and the Individual Defendants are collectively referred to herein as “Defendants”.

NATURE OF THE CASE

1. This case alleges that Defendants misrepresented to investors that Alnylam's Phase 3 clinical trial for its highly-anticipated blockbuster drug Patisiran (APOLLO III), supported a broad-based FDA label to treat polyneuropathy *and* cardiomyopathy manifestations of a rare disease known as Hereditary Transthyretin-Mediated ("hATTR") Amyloidosis, or, at a bare minimum, the inclusion of purportedly positive cardiac data from the trial on Patisiran's label that would broaden the drug's intended patient population as well as its commercial potential for the Company. Defendants knew or recklessly disregarded that APOLLO III was not designed to support the safety or efficacy of Patisiran for cardiomyopathy or cardiac manifestations of hATTR Amyloidosis, and, as such, that it was impossible that the FDA would approve a broad-based label for the drug or even allow cardiac data to be included on Patisiran's label when APOLLO III lacked, as the FDA later stated, "any cardiac efficacy data".

2. By deceiving the market in this way, Defendants artificially inflated the value of Alnylam securities during the Class Period and unloaded approximately **\$66 million** worth of their personal holdings of Alnylam stock at these inflated prices – as well as at suspicious times and in suspicious quantities. Indeed, the Individual Defendants sold \$21 million worth of their Alnylam stock in a three-week period between October 30, 2017 and November 22, 2017, right around Alnylam's November 2, 2017 announcement that the Company had finished analyzing the APOLLO III data – which, as discussed below, apprised Defendants of serious safety concerns that were later flagged by the FDA. At the same time, Defendants raised approximately **\$800 million** for the Company through its November 14, 2017 secondary public offering ("SPO"). The truth about Patisiran was revealed as Defendants disclosed that the FDA had strictly limited the Patisiran label to polyneuropathy and allowed no cardiac data from the trial to be included on the

label because the FDA found that APOLLO III “*does not provide any cardiac efficacy data*” and raises “*serious*” cardiac safety concerns about Patisiran.² On this news, revealed through two public disclosures, Alnylam’s stock fell in value, erasing approximately \$1.2 billion in market capitalization, and damaging Plaintiff and the Class.

3. According to its website, Alnylam is a global biopharmaceutical company that develops novel therapeutics based on RNA interference (“RNAi”). Alnylam’s pipeline of investigational RNAi therapeutics is focused in three Strategic Therapeutic Areas, or “STArS”: Genetic Medicines; Cardio-Metabolic Diseases; and Hepatic Infectious Diseases. Prior to the start of the Class Period, Alnylam had no FDA-approved drugs on the market, and the Company was in the process of developing three investigational RNAi therapeutic candidates to treat hATTR Amyloidosis, which, at that time, had no FDA-approved drug treatments on the market.

4. Individuals suffering from hATTR Amyloidosis typically require treatment for polyneuropathy (nerve-related disease), cardiomyopathy (heart disease), or both neuro and cardio manifestations of the disease. hATTR Amyloidosis is difficult to diagnose. As a result, drug companies developing treatments for hATTR Amyloidosis, like Alnylam, spend a substantial amount of resources educating physicians, including neurologists and cardiologists, on how to diagnose the disease. The FDA label on a drug profoundly influences the range of doctors that a drug company can market its respective drug treatment to. Notably, over 50% of hATTR Amyloidosis cases concern cardiac manifestation of the disease, making the treatment of cardiac manifestations key to capturing the small (approximately 50,000 worldwide) but lucrative (approximately \$450,000 per patient per year) hATTR Amyloidosis patient population.³

² All emphasis is added unless otherwise noted.

³ See November 2, 2017 Alnylam Conference Call to Discuss APOLLO Phase 3 study of Patisiran Results at 8.

5. Starting before the Class Period, Alnylam was developing three hATTR treatments: Patisiran, Revusiran, and ALN-TTRsc02. Alnylam intended Patisiran and ALN-TTRsc02 to treat hATTR patients with polyneuropathy (each through different deliveries), and Revusiran to treat hATTR patients with cardiomyopathy. However, as set forth herein, those plans changed when Alnylam abruptly had to pull the plug on Revusiran after four times as many cardiac patients died on the drug compared to placebo cardiac patients.

6. After ending the Revusiran trial, the Individual Defendants tried to salvage Alnylam's footing in the hotly-contested race to be first to market an FDA-approved hATTR Amyloidosis drug treatment, and particularly one that could address the broadest patient population, by changing the narrative on Patisiran. To that end, during the Class Period they trumpeted the drug's safety and efficacy in treating both polyneuropathy *and* cardiomyopathy manifestations of hATTR Amyloidosis. Specifically, with increasing intensity, Defendants materially misled the market into believing that, based on the results of APOLLO III, the FDA would approve a broad-based label for treatment of polyneuropathy and cardiomyopathy manifestations of hATTR Amyloidosis, or, at a minimum, would allow Alnylam to include promising cardiac data from the trial on the drug's anticipated label.

7. The Class Period begins on September 20, 2017, when Alnylam announced that it received the data from APOLLO III. The data was not made public at that time, but the Individual Defendants discussed it in the abstract during an investor conference call. Specifically, the Individual Defendants announced the topline results for APOLLO III, including, *inter alia*, that Patisiran hit its primary (polyneuropathy) endpoint and that "the positive effect of patisiran on mNIS+7 [a metric relating to the polyneuropathy endpoint] was also seen in patients in the cardiac subgroup, which is an important result." After this announcement and related commentary that

ensued, Alnylam's stock skyrocketed by about 51% – from a close of \$75.04 per share on September 19, 2017 to close at \$113.84 per share on September 20, 2017.

8. Unbeknownst to investors, however, the APOLLO III data actually (i) showed that there were seven cardiac deaths in Patisiran versus only one in cardiac death in placebo (which is statistically similar to the cardiac safety profile witnessed in the failed Revusiran study);⁴ and (ii) provided *no* cardiac efficacy data upon which Alnylam could obtain a broad-based FDA label or even cardiac data on the label.

9. Also on September 20, 2017, a Leerink Partners analyst hosted a conference call with a specialist to discuss Alnylam's data announcement. The specialist noted that he would be looking for "any biomarker data indicative of cardiac improvement." Leerink Partners further noted that any potential market share in cardiac amyloidosis patients would represent a "major pivot point in [their] model" for Alnylam.

10. The excitement generated by Defendants over Patisiran's potential to mitigate Revusiran's failure was palpable. A securities analyst from BMO Markets in a September 21, 2017 report titled "Raising PT On APOLLO Strength," commented, in relevant part, that "based on management comments [on APOLLO III], we also assume adoption [of Patisiran] in cardiomyopathy (CM) patients as mNIS+7 benefit was seen in the CM subgroup and many hATTR patients have a mixed phenotype." Similarly, a securities analyst from JP Morgan in a September 20, 2017 report titled "APOLLO Phase 3 Hits Best Case Scenario", stated that the key questions on the September 20, 2017 topline results call would focus on, among other things: (i) Patisiran

⁴ Because there were twice as many Patisiran patients as placebo patients in APOLLO III, the drug to placebo death ratio was really 3.5:1 rather than 7:1 – very close to the 4:1 ratio for Revusiran that halted that trial.

activity in cardiomyopathy patients; (ii) the potential breadth of the Patisiran label; and (iii) what additional analyses could be presented at an ATTR Amyloidosis meeting in November.

11. After digesting the top-line results, the market eagerly anticipated Alnylam's deeper dive into the APOLLO III results, which was due to be reported in November 2017. On November 2, 2017, the Individual Defendants gave the market that deeper analysis when they hosted a conference call to discuss their complete review of the APOLLO III data. This call was hosted by Defendant Maraganore and involved significant participation from Defendant Vaishnaw. During the call, these two defendants touted the results of APOLLO III vis a vis the drug's primary endpoint of polyneuropathy, and repeatedly emphasized that the APOLLO III data also included "positive, statistically significant results on a key exploratory cardiac biomarker and echocardiographic endpoints in the cardiac subpopulation". These and similar comments concerning Patisiran's potential to also benefit patients with cardiac manifestations of hATTR Amyloidosis further intensified the excitement about the drug's blockbuster potential and its potential to obtain a broad-based label from the FDA and/or inclusion of Cardiac data on the drug's label.

12. Notably, in or around the time of Alnylam's review of the APOLLO III data – which the Company stated was complete as of November 2, 2017 – the Individual Defendants also learned, but did not publicly address, that there were 7 Patisiran cardiac deaths while there was only 1 cardiac death for the placebo. After Alnylam's troubling experience with Revusiran – which trial was halted because it demonstrated a 4:1 drug to placebo death ratio – the Individual Defendants knew (or were reckless in not knowing) that Patisiran's 3.5:1 drug to placebo death ratio posed serious safety issues relating to cardiac patients, militating against FDA approval of a dual label, or even cardiac data on the drug's label. The Individual Defendants, however, did not

address these serious safety concerns with the market at that time. Instead, they unloaded \$21 million of their Alnylam stock after learning of the serious safety issues with cardiac deaths in APOLLO III.

13. Thereafter, Individual Defendants still continued to represent that the APOLLO III data demonstrated both Patisiran's safety and efficacy with respect to cardiac patients. Worse, as the FDA later described in a report released in September 2018, Alnylam also tried to downplay the serious adverse cardiac events by attempting to switch the classification of two placebo deaths to cardiac-related to lower the drug to placebo death ratio.⁵ The FDA disagreed with Alnylam's attempt, stating that the two deaths the Company characterized as cardiac-related were really stroke-related.

14. Defendants submitted Patisiran's New Drug Application ("NDA") to the FDA on a rolling basis in November 2017, completing its filing in December 2017. Following the completion of the NDA submission in January 2018, certain defendants hosted an Investor Lunch at the JP Morgan Healthcare Conference, during which they continued to fuel market excitement about Patisiran's dual potential. At the conference, these defendants claimed, in relevant part, that: (i) hATTR Amyloidosis is largely a mixed-phenotype disease, *i.e.* that patients with polyneuropathy most often also have cardiomyopathy; (ii) the APOLLO III data supported the safety and efficacy of Patisiran for patients with cardiac manifestations of hATTR Amyloidosis; and (iii) Patisiran had the potential to achieve a broad-based FDA label. Not surprisingly, therefore, a JP Morgan analyst reporting on the investor lunch stated, in relevant part, that: "Patisiran Label: Given hATTR being a multi-system disease and the spectrum of benefit observed

⁵ By raising the number of cardiac deaths in the placebo group, Alnylam was trying to bring the amount of cardiac placebo deaths up near the amount of cardiac Patisiran deaths.

with patisiran (autonomic, neuro, cardiac, etc.) relative to placebo, Alnylam believes it has a strong argument to secure a broad hATTR label, one that would enable active promoting to cardiologists.” As noted *supra*, Alnylam’s ability to market Patisiran to cardiologists would open a substantial market to Alnylam that was previously lost by Revusiran’s failure.

15. In early February 2018, the FDA accepted Alnylam’s NDA and granted its request for priority review, stating that it would give the Company a decision by August 2018.

16. For the remainder of the Class Period, analysts continually asked the Individual Defendants about the Patisiran label, and whether Defendants anticipated a broad-based label that included cardiac data. On analyst call after analyst call, the Individual Defendants repeatedly, explicitly, and confidently touted a broad label and claimed, at a minimum, that the inclusion of cardiac data was viable and even likely for Patisiran. It was neither, however, and the Individual Defendants knew it.

17. The Individual Defendants are medical doctors and/or highly educated PhDs and/or are well acquainted with FDA trials and, as such, were well aware that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) as of, at the latest, there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label. Indeed, the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

18. While pumping the price of Alnylam stock up, the Individual Defendants unloaded tens of millions of dollars of their Alnylam shares reaping substantial profits at the market's expense. In total, the Individual Defendants sold approximately **\$66 million dollars** of Alnylam securities – about \$21 million of which they suspiciously sold in a concentrated three-week period between October 30, 2017 and November 22, 2017 – right when they completed their review of the APOLLO III data and, thus, knew material, nonpublic, adverse information about the efficacy and safety of Patisiran for truly cardiac patients for truly cardiac patients. Alnylam also issued **\$800 million** of Alnylam securities to the public at this time through a November 14, 2017 SPO.

19. On August 10, 2018, the fraud began to be revealed. On that date, the Company announced that the FDA had determined that Patisiran would only receive a label for the treatment of polyneuropathy – and not cardiomyopathy – and that Alnylam could not even include cardiac data from APOLLO III on the Patisiran label. After the Individual Defendants' rosy statements about a "broad" Patisiran label (meaning for both cardiomyopathy and polyneuropathy) or that cardiac data, at a minimum, would be included on the label, the market was taken aback. Alnylam's stock price fell approximately 6%, from \$97.38 on August 10, 2018, to close at \$90.95 on August 13, 2018.

20. Defendants tried to distract the market, *inter alia*, by continuing to tout the positive data received from APOLLO III, including the cardiac data from the study, by reassuring the market that they would continue to discuss a broader label for Patisiran with the FDA, and that the potential for a broader FDA label was still in the works. This distraction worked temporarily, but on September 12, 2018, the other shoe dropped. On that date, multiple analysts published reports analyzing a voluminous 485-page FDA report on APOLLO III that had just been released (the

“FDA Report”),
(https://www.accessdata.fda.gov/drugsatfda_docs/nda/2018/210922Orig1s000MultiR.pdf).

21. The FDA Report contained new damning details about Patisiran’s safety and efficacy, including flatly stating that Alnylam did not provide “any cardiac efficacy data” and that the FDA had “serious” concerns about the cardiac deaths witnessed in the trial. In other words, according to the FDA, Alnylam had no support for Patisiran’s efficacy in treating cardiac manifestation of hATTR Amyloidosis, there were serious safety concerns over the drug to placebo cardiac patient death ratio, and, thus, Defendants had to go back to the drawing board to design a completely new study that could test the drug’s potential safety and efficacy for treating cardiac patients. For the first time, therefore, the market fully appreciated that Defendants had no basis for their bullishness on Patisiran to treat cardiac manifestations of hATTR Amyloidosis, and that there was no real timeline for gaining FDA-approval for a broader label for Patisiran. This left Alnylam’s competitor, Pfizer, Inc., with a clear path to come to market first with its drug, Tafamadis, to treat the hATTR Amyloidosis patient population suffering from cardiomyopathy. On this news, Alnylam’s stock price plunged another \$5.60, or over 5.5%, to close at \$94.75 per share on September 12, 2018.

22. Eight months later, in May 2019, Alnylam lost the race to be the first company to bring an hATTR cardiomyopathy drug to market, as the FDA approved Pfizer’s hATTR drug, Tafamidis, for the treatment of cardiomyopathy. If it is even possible to achieve, it will likely take years for Alnylam to gain FDA approval for a broader label for Patisiran to treat cardiac manifestations of hATTR Amyloidosis, and by then it will require a major uphill battle for the Company to recapture market share from Tafamidis, Pfizer’s already-established drug.

23. Alnylam investors lost hundreds of millions of dollars as a result of the alleged fraud set forth herein.

JURISDICTION AND VENUE

24. The claims asserted herein arise under Sections 10(b) and 20(a) of the Exchange Act (15 U.S.C. §§ 78j(b) and 78t(a)) and SEC Rule 10b-5 promulgated thereunder (17 C.F.R. § 240.10b-5), giving this Court jurisdiction over the subject matter of this action pursuant to 28 U.S.C. § 1331, and Section 27 of the Exchange Act (15 U.S.C. § 78aa).

25. Venue is proper in this Judicial District pursuant to 28 U.S.C. § 1391(b) and Section 27 of the Exchange Act. Substantial acts in furtherance of the alleged fraud or the effects of the fraud have occurred in this Judicial District. Many of the acts charged herein, including the dissemination of materially false and misleading information occurred in substantial part in this Judicial District. In addition, the Company's principal executive offices are located within this Judicial District.

26. In connection with the acts, transactions and conduct alleged herein, Defendants directly and indirectly used the means and instrumentalities of interstate commerce, including the United States mail, interstate telephone communications and the facilities of a national securities exchange.

PARTIES

27. Lead Plaintiff Tunc Toker, as set forth in the certification previously attached to his motion for appointment as lead plaintiff, purchased Alnylam securities during the Class Period, and suffered damages as a result of the federal securities law violations and the materially false and/or misleading statements and/or material omissions alleged herein.

28. Defendant Alnylam is incorporated in Delaware and its principal executive offices are located at 3000 Third Street, Cambridge, Massachusetts 02142. The Company's securities are traded on the NASDAQ under the symbol "ALNY."

29. Defendant John M. Maraganore has served as the Chief Executive Officer of Alnylam at all relevant times. Defendant Maraganore has his Masters of Science and PhD in biochemistry and molecular biology from the University of Chicago. Defendant Maraganore has invented and led the discovery and development efforts for other drugs while he was a Director of Market and Business Development at Biogen Inc. Throughout the Class Period, while he participated in the scheme to artificially inflate Alnylam's stock price, Defendant Maraganore sold \$24.2 million of his personal holdings of Alnylam common stock.

30. Defendant Manmeet S. Soni has served as the Chief Financial officer ("CFO") of Alnylam at all relevant times. Defendant Soni graduated from Hansraj College at Delhi University in India, and previously served as the Chief Financial Officer and Treasurer of ARIAD Pharmaceuticals, Inc.

31. Defendant Yvonne L. Greenstreet was Alnylam's Chief Operations Officer ("COO") and Executive Vice President ("EVP"). Defendant Greenstreet received her medical degree (MBChB) from the University of Leeds, UK, and an MBA degree from INSEAD in France. Throughout the Class Period, while she participated in the scheme to artificially inflate Alnylam's stock price, Defendant Greenstreet sold \$1.3 million of her personal holdings of Alnylam common stock.

32. Defendant Akshay K. Vaishnaw was Alnylam's EVP of Research & Development and, later, the President of Research & Development. Defendant Vaishnaw received his MD from the University of Wales College of Medicine, UK and his PhD from the University of London,

UK. Prior to joining Alnylam, Defendant Vaishnaw was involved in many aspects of clinical research and business development at Biogen Inc., where Defendant Maraganore also previously worked. Throughout the Class Period, while he participated in the scheme to artificially inflate Alnylam's stock price, Defendant Vaishnaw sold \$16.7 million of his personal holdings of Alnylam common stock.

33. Defendant Barry Greene is Alnylam's President. Defendant Greene received his Bachelors of Science degree in Industrial Engineering from the University of Pittsburgh. Prior to joining Alnylam, Barry Greene was the General Manager of Oncology at Millenium Pharmaceuticals, Inc. Throughout the Class Period, while he participated in the scheme to artificially inflate Alnylam's stock price Defendant Greene sold \$24 million of his personal holdings of Alnylam common stock.

34. As noted *supra* in footnote 1, Defendants Maraganore, Soni, Greenstreet, Vaishnaw, and Greene are collectively referred to as the Individual Defendants.

35. The Individual Defendants possessed the power and authority to control the contents of Alnylam's SEC filings, press releases, and other market communications. The Individual Defendants were provided with copies of the Company's SEC filings and press releases alleged herein to be misleading prior to or shortly after their issuance and had the ability and opportunity to prevent their issuance or to cause them to be corrected. Because of their positions with the Company, their educational and experiential backgrounds, and their access to material information available to them but not to the public, the Individual Defendants knew that the adverse facts specified herein had not been disclosed to and were being concealed from the public, and that the positive representations being made were then materially false and misleading. The

Individual Defendants are liable for the materially false and misleading statements and omissions pleaded herein.

FACTUAL ALLEGATIONS

A. Background about Alnylam and hATTR

36. According to its website, Alnylam is a global biopharmaceutical company that develops novel therapeutics based on RNAi. RNAi is a naturally occurring biological pathway within cells for sequence-specific silencing and regulation of gene expression. Alnylam purports to harness the RNAi pathway to develop a new class of innovative medicines, known as RNAi therapeutics. RNAi therapeutics are comprised of small interfering RNA, or siRNA, and function upstream of today's medicines by potentially silencing messenger RNA or mRNA, that encode for disease-causing proteins, thus preventing them from being made.

37. Alnylam's pipeline of investigational RNAi therapeutics is focused in three Strategic Therapeutic Areas, or "STArS": Genetic Medicines; Cardio-Metabolic Diseases; and Hepatic Infectious Diseases. During the Class Period, Alnylam trumpeted its commitment to its "Alnylam 2020 strategy," which was supposed to achieve three marketed products and ten RNAi therapy clinical programs, including four in late stages of development, across its three STArS by the end of 2020.

38. hATTR Amyloidosis is a rare, progressively debilitating and often fatal disease that affects approximately 50,000 patients worldwide. The disease is caused by the deposition of wild-type and mutant transthyretin, or TTR in peripheral tissues, such as the nerves, heart and gastrointestinal tract. TTR protein is produced primarily in the liver and is normally a carrier of Vitamin A. The two cardinal manifestations of the disease are polyneuropathy and cardiomyopathy with many patients exhibiting both manifestations. The majority of hATTR

patients have cardiomyopathy or cardiac manifestations of hATTR Amyloidosis. According to Alnylam, Patisiran targets wild-type and all known mutant forms of TTR and represents a potential therapeutic approach for the treatment of hATTR Amyloidosis.

39. Prior to the start of the Class Period, Alnylam had three investigational RNAi therapeutic drugs in clinical trials for treatment of hATTR Amyloidosis: Patisiran, Revusiran, and ALN-TTRsc02. Revusiran was intended to treat patients with cardiomyopathy and Patisiran and ALN-TTRsc02 were intended to treat patients with polyneuropathy. Patisiran and Revusiran were both in Phase 3 clinical trials prior to the start of the Class Period. The Phase 3 trial for Revusiran was called “ENDEAVOUR”, and the Phase 3 trial for Patisiran was called “APOLLO III”. These two drugs, which had the potential to be the first FDA-approved drug treatments on the market for cardiomyopathy and polyneuropathy, respectively, were widely anticipated to be blockbuster drugs for Alnylam. Accordingly, securities analysts closely followed the two Phase 3 studies. For example, a Morgan Stanley analyst in a report dated August 2, 2016 noted that Alnylam’s lead drugs – Revusiran and Patisiran – were the “key driver[s] behind [Morgan Stanley’s] base-case scenario valuation.”

40. Based on the anticipated results of these two clinical trials, Alnylam planned to seek FDA approval for a new drug label for each of the two drugs so that the Company could bring them to market and finally transform itself from a research & development company to a commercialized company.

41. The Code of Federal Regulations provides the specific rules for applications for FDA approval to market a new drug (21 CFR 314). Notably, the FDA will refuse to approve a new drug or an indication for a drug if “[t]here is a lack of substantial evidence consisting of adequate and well-controlled investigations, as defined in §314.126, that the drug product will

have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in its proposed labeling” (21 CFR 314.125). Concerning labeling, 21 CFR 314.126(b) further states, in relevant part, that “all indications listed in the INDICATIONS AND USAGE section [of the proposed labeling] *must be supported by substantial evidence of effectiveness based on adequate and well-controlled studies.*”

42. Alnylam, and other pharmaceutical companies, provide the FDA with evidence from clinical trials to support labeling for its drugs. Clinical trials have three kinds of endpoints: primary, secondary and exploratory. The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use provides guidelines that drug regulators across the world have adopted (including the FDA). Guideline “E9” addresses “Statistical Principles for Clinical Trials”

43. E9 distinguishes between “primary” and “secondary” clinical trial endpoints. The primary endpoint “should be the variable capable of providing the most clinically relevant and convincing evidence directly related to the primary objective of the trial.” Secondary endpoints “are either supportive measurements related to the primary objective or measurements of effects related to the secondary objectives.” Exploratory endpoints are generally not used to support drug labeling.⁶ Indeed, the E9 guideline does not even mention the notion of an “exploratory endpoint”. The FDA’s own guideline on multiple endpoints does mention exploratory endpoints, but mainly states that they “are included [in clinical trials] to explore new hypotheses,” and not to guide regulatory actions such as the approval for FDA labels. <https://www.fda.gov/media/102657/download>.

⁶ See Marks, Ron, Navigating Regulatory Biostatistical Requirements During Trial Analysis and Submission: Post Hoc Analyses, Clinipace, July 1, 2015 (<https://www.clinipace.com/navigating-regulatory-biostatistical-requirements-during-trial-analysis-and-submission-post-hoc-analyses/>).

44. In APOLLO III, no cardiac outcome was included as either a primary or secondary outcome. As later noted by an FDA reviewer: “Study ALN-TTR02-004 [APOLLO III] does not provide any cardiac efficacy data.” What this reviewer meant is that if an outcome is not included as a primary or secondary outcome in the study design, no meaningful data that could inform a regulatory decision will emerge. The same reviewer also noted that “there were two open-label extension studies in which echocardiography and NT-proBNP were measured that showed no meaningful differences in these measures with 18 to 24 months of follow-up.” Thus, even if the cardiac-related endpoints had been designed in to the original study as primary, the data would not have supported a cardiac labeling.

B. Alnylam Abruptly Halts its ENDEAVOUR Phase 3 Trial For Revusiran Due to a 4:1 Drug to Placebo Death Ratio Among Cardiac-Related Patients

45. In October 2016, Alnylam’s (and its investors’) hopes of bringing Revusiran to market to treat hATTR Amyloidosis patients with cardiomyopathy were dashed. At that time, Alnylam was forced to discontinue the ENDEAVOUR Phase 3 clinical trial because the mortality rate in the study was 16:2 – with Revusiran responsible for 16 deaths and the placebo responsible for only two. Notably, because the ENDEAVOUR study had twice as many Revusiran patients as placebo patients in it, the actual death ratio reflected in the trial data was 4:1. In light of the foregoing, Alnylam’s Data Monitoring Committee (“DMC”) recommended that the Company halt the ENDEAVOUR trial because the risk/benefit no longer supported proceeding with the trial.

46. After announcing the devastating failure of the ENDEAVOUR trial, Alnylam’s stock plummeted from \$78.60 on October 5, 2016 to \$34.27 on October 7, 2016 - a drop of approximately 56%.

47. On this news, several securities analysts downgraded Alnylam’s stock rating and lowered their price targets for its common stock. For example, on October 6, 2016, a Barclays

analyst downgraded Alnylam's price target by approximately 41% from \$85 to \$50. A Morningstar analyst likewise decreased the "fair value estimate" for Alnylam by approximately 44% from \$90 to \$50. Further, an October 7, 2016 Morgan Stanley report titled "Revusiran Discontinuation Raises Key Questions; Downgrading to EW" removed Revusiran from the model for Alnylam, causing Morgan Stanley to downgrade the stock rating to equal-weight, and decrease the price target from \$93 to \$36, a decrease of approximately 61%.

C. Patisiran's APOLLO III Clinical Trial and Its Importance for Alnylam

48. APOLLO III for Patisiran was always important to Alnylam and its investors, but it became even more important when the ENDEAVOUR trial for Revusiran failed in October 2016. Alnylam initiated APOLLO III in November 2013 and completed it in September 2017. APOLLO III was a random double-blind placebo-controlled trial designed to evaluate the efficacy and safety of Patisiran in hATTR amyloidosis neuropathy patients. Patients were randomized two-to-one Patisiran-to-placebo, meaning for every one patient that received the placebo two patients received Patisiran.

49. APOLLO III had three sets of objectives: primary, secondary, and exploratory. The single primary APOLLO III objective related to neuropathy; namely, to determine the efficacy of Patisiran by evaluating the difference between the Patisiran and placebo groups in the change from baseline of "mNIS+7" (modified neuropathy impairment score +7) at 18 months.⁷ The secondary objectives, which were all likewise related to neuropathy, were designed to determine the effect of

⁷ See APOLLO: A Phase 3 Multicenter, Multinational, Randomize, Doubleblind, Placebo-controlled Study to Evaluate the Efficacy and Safety of ALN-TTR02 in Transthyretin (TTR)-Mediated Polyneuropathy (Familial Amyloidotic Polyneuropathy-FAP) Protocol Version 6, 08 September 2015 (available at https://clinicaltrials.gov/ProvidedDocs/48/NCT01960348/Prot_000.pdf) ("APOLLO Protocol") at 40-42.

Patisiran on various clinical parameters, including the Norfolk Quality of Life-Diabetic Neuropathy Questionnaire, the NIS-weakness score; the modified Body Mass Index; timed 10-meter walk test; and the Autonomic symptoms questionnaire, by assessing the difference between Patisiran and the placebo in the change from baseline for the aforementioned measures at 18 months. The exploratory objectives of APOLLO III were designed to determine the difference between the Patisiran and placebo groups in the change from baseline in approximately ten different tests. One of those tests was a cardiac assessment through echocardiogram, troponin I, and N terminal prohormone of B-type natriuretic peptide (“NT-proBNP”) levels.⁸

50. Patients participated in APOLLO III for approximately 21 months and were screened within 42 days prior to the administration of the study drug. Eligible patients were randomized to receive either Patisiran or the placebo once every 21 days for 78 weeks. The blinded study drug was administered as a 70 minute IV infusion. A DMC was implemented for the study and operated under a pre-specified charter.

51. Safety was assessed throughout the study by collecting adverse events (“AEs”) and Serious Adverse Events (“SAEs”). An AE is defined as any untoward medical occurrence in a patient or clinical investigational patient administered a pharmaceutical product and which does not necessarily have a causal relationship with the treatment. A SAE is defined as any untoward medical occurrence that at any dose: (i) results in death; (ii) is life-threatening; (iii) requires inpatient hospitalization or prolongation of existing hospitalization; (iv) results in persistent or significant disability/incapacity; (v) is a congenital anomaly or birth defect; (vi) an important medical event that may not be immediately life-threatening or result in death or hospitalization but

⁸ APOLLO Protocol at 40.

may jeopardize the patient or may require intervention to prevent one of the other outcomes listed in items (i)-(v).⁹

52. APOLLO III was a critical trial for Alnylam because the Company did not yet have a single RNAi drug in the market, and Patisiran, if approved, had the potential to be the first drug for treatment of hATTR Amyloidosis, giving Alnylam a distinct market advantage, particularly if it could capture the broadest patient population suffering from hATTR Amyloidosis. Although rare (approximately 50,000 suffer from the disease worldwide), the approximate cost for Patisiran per patient was estimated to be approximately \$450,000 per patient per year, demonstrating the blockbuster potential for the drug.

53. As set forth herein, at a very basic level, APOLLO III was not designed to study the effects of Patisiran on patients with cardiac manifestations of hATTR Amyloidosis. Indeed, the FDA stated that APOLLO III “does not provide any cardiac efficacy data”. Instead, the Individual Defendants convinced the market that the nature of hATTR Amyloidosis and the way it is expressed in patients (i.e., in mixed phenotypes) would allow Alnylam to include cardiac data from APOLLO III on the label. But that was not the case. The failure by the Individual Defendants to include any cardiac efficacy data or any primary or secondary cardiac endpoints made it impossible that the FDA would approve a Patisiran label with cardiac data on it.

54. Analysts confronted the Individual Defendants with questions regarding this exact point but the Individual Defendants were quick to sidestep them and reiterate their confidence in Patisiran’s dual potential. For example, on a February 8, 2018, earnings call a Sanford C. Bernstein Analyst asked “[w]ould it matter at all that there wasn’t a primary endpoint focused on sort of cardiac and that primary was much more focused on the neuropathy?” Defendant Vaishnaw,

⁹ APOLLO Protocol at 84-88.

instead of disclosing to the market that getting FDA approval for cardiomyopathy without any cardiac efficacy data or a primary cardiomyopathy endpoint was impossible, stated that “[w]e feel, and I think most people will agree with, that the fact that the cardiac outcomes weren’t the primary endpoint is not the issue here.”

D. During the Class Period, Alnylam Raced Against Pfizer and Ionis to be the First Company to Bring an hATTR Amyloidosis Drug to Market

55. Throughout the Class Period, Alnylam was in a heated race against Pfizer and Ionis to be the first company to bring an hATTR Amyloidosis drug to market.

56. Ionis submitted its NDA to the FDA for its hATTR Amyloidosis drug, Tegsedi, in November 2017 to treat polyneuropathy.

57. Alnylam submitted its NDA to the FDA for Patisiran in December 2017.

58. On March 29, 2018, Pfizer reported that its hATTR Amyloidosis drug, Tafamidis, succeeded in its Phase 3 trial, causing Alnylam stock to fall by over 25%.

59. On January 14, 2019, Pfizer submitted its Tafimidis NDA to the FDA.

60. In May 2019, the FDA approved Pfizer’s Tafimidis for use in hATTR cardiomyopathy patients, making Pfizer the first company to bring such a drug to market.

E. Defendants Receive the Much Anticipated APOLLO III Data and Change the Narrative on Patisiran, Misleading the Market about the Drug’s Dual Potential to Treat Polyneuropathy and Cardiomyopathy

61. In or around September 2017, Defendants received the data for the much-anticipated APOLLO III study. On September 20, 2017, Alnylam presented topline results of the study to the public, but did not release the data to the public. According to Defendants, the APOLLO III data showed that the primary and secondary endpoints of the study were met supporting that Patisiran likely would be approved for polyneuropathy. Rather than end the story there, however, Defendants sought to reverse the devastating harm caused by Revusiran’s failure,

inter alia, by beginning to stir up the market's excitement about potentially getting a broader FDA label than originally intended for Patisiran, or, at a minimum, getting exploratory cardiac data from APOLLO III on the Patisiran label.

62. To convince the market that securing a FDA approval for a broad label was likely, the Individual Defendants increasingly began to blur the lines between the treatment of cardiomyopathy and neuropathy manifestations of hATTR Amyloidosis. On November 29, 2017, a Piper Jaffray analyst stated: "I want to tease out a little bit more about what you're talking about on the cardiac side, because while the study really was enrolled primarily polyneuropathy patients, sort of the lines have really blurred with traders. So tell us a little bit about what you think the ultimate label..." The Individual Defendants wanted these lines blurred so they could convince the market that the FDA would approve a dual neuropathy/cardiomyopathy label or at a minimum have cardiac data on the label – and so they could raise \$800 million for the Company and sell approximately \$66 million of Alnylam common stock.

63. As set forth *infra*, securities analysts and Alnylam investors took the bait, and Patisiran's potential to also treat hATTR Amyloidosis patients with cardiac manifestations immediately became a focal point of Alnylam conference calls and investor presentations thereafter.

F. The Individual Defendants Announce on November 2, 2017 That They Completed Their Analysis of the APOLLO III Data

64. On November 2, 2017, Alnylam announced that it had fully analyzed the APOLLO III data it had received on September 20, 2017:

Alnylam...announced today *positive complete results* from the APOLLO Phase 3 study of patisiran...

Cardiac Subpopulation Results

Favorable and significant changes in several exploratory cardiac measures, including N-terminal pro b-type natriuretic peptide (NT-proBNP), certain echocardiographic parameters, and 10-MWT were reported in patisiran-treated patients in the pre-specified cardiac subpopulation*....

Safety and Tolerability

Patisiran showed an encouraging safety and tolerability profile relative to placebo with up to 18 months of dosing. Specifically...

The incidence of SAEs across the patisiran (36.5 percent) and placebo (40.3 percent) groups was similar....

Patisiran also showed an encouraging tolerability profile in the pre-specified cardiac subpopulation, with a similar frequency of AEs in the patisiran and placebo arms and a numerically lower incidence of SAEs (34.4 percent for patisiran versus 50.0 percent for placebo). The frequency of deaths was 5.6 percent for patisiran versus 11.1 percent for placebo.

65. Following this announcement, the price of Alnylam stock closed at \$133.59 from an open of \$121.34 per share, an increase of approximately 10%.

66. At this point, at the very least, the Individual Defendants knew or recklessly disregarded all the specifics about the data, including that there were 7 cardiac deaths on Patisiran and only 1 cardiac death on the placebo, or a 3.5 to 1 drug to placebo death ratio after accounting for the fact that there twice as many Patisiran patients as placebo patients in APOLLO III. The Individual Defendants also knew that Alnylam halted the Revusiran trial because of a 4:1 drug to placebo death ratio substantially similar to the 3.5 to 1 Patisiran ratio.

G. Alnylam Submits the Patisiran NDA to the FDA

67. In November 2017, the Company submitted the Patisiran NDA to the FDA on a rolling basis, completing its submission in December 2017. In February 2018, the FDA accepted the NDA and stated that it would give it priority review and make a determination on the NDA by August 2018.

H. The Individual Defendants Unload \$66 Million in Alnylam Stock

68. During the Class Period, while Alnylam stock was artificially propped up by the Individual Defendants' misleading statements, these defendants sold \$66 million of their Company stock at suspicious times and in suspicious amounts. As alleged below, \$24 million of their sales were concentrated in a 3 week period – right at the time Alnylam completed its analysis of the APOLLO III data which showed serious safety concerns surrounding the drug to placebo cardiac patient death ratio.

I. The Individual Defendants Raise \$800 Million While Alnylam Stock is Artificially Inflated

69. Also while Alnylam's stock price was artificially propped up by Defendants' misstatements, Defendants raised over \$800 million in a secondary stock offering in the November 14, 2017 SPO.

J. After Submitting the Patisiran NDA, Alnylam Tried to Re-Classify Two Cardiac-Related Deaths in APOLLO III

70. While discussing the Patisiran NDA with the FDA after its December 2017 submission, Alnylam tried to re-characterize the data to make the cardiac safety issue with Patisiran go away. The FDA later stated in its August 10, 2018 report (which was not released until on or around September 7, 2018) that, apparently after the FDA raised concerns with the Company over the high number of cardiac deaths on Patisiran compared to the placebo, Alnylam tried to re-classify two placebo as cardiac-related:

Originally, all 7 deaths in the patisiran group (4.7%) were considered to be cardiovascular in nature, with only 1 cardiovascular death in placebo-treated patients (1.3%). The applicant subsequently convened an independent and blinded adjudication committee to review the cases of death from Study 004 and classify them as cardiovascular or non-cardiovascular.... With adjudication, all 7 deaths in the patisiran group remained attributed to cardiovascular causes, *whereas the causes of death for 2 patients in the placebo group were reclassified from non-cardiovascular to cardiovascular*

...(increasing the total number of cardiovascular deaths to 3 in the placebo group (3.9%). (Emphasis added).

71. Significantly, the FDA disagreed with Alnylam's determination, finding that the reclassifications were unsupported:

Importantly, however, both of the cardiovascular deaths added to the placebo group were attributed to stroke, not heart failure.... Thus, with respect to deaths plausibly related to heart failure, the 7 to 1 difference (4.7% in the patisiran group vs. 1.3% in the placebo group) remains, and this difference is concerning.

See also id. at 176 (“these deaths were notably caused by strokes and not CHF [congestive heart failure] or arrhythmias. All of the patisiran deaths were related to CHF or arrhythmias. Therefore, the deaths due to cardiac causes such as CHF or arrhythmia remain at 7 (4.7%) to 1 (1.3%) in the drug versus placebo comparison”).

K. The Market Learns the Truth

72. On August 10, 2018, Alnylam revealed that the FDA had denied its application to treat cardiomyopathy patients or patients with cardiac manifestations of hATTR amyloidosis with Patisiran. The FDA also denied the Company's application to put cardiac data on a Patisiran label. The FDA did approve Patisiran for hATTR polyneuropathy treatment, but the market was expecting – on the basis of the Individual Defendants' many months of positive statements – a dual label, or at the very least purportedly promoting cardiac data from APOLLO III on the Patisiran label. Thus, Alnylam's stock fell over 5% on this news.

73. The Individual Defendants nevertheless continued to tout the APOLLO III data including cardiac data, and told analysts that they would continue to talk with the FDA about achieving a broad Patisiran label in the future.

74. On September 12, 2018, the market learned the full extent of Alnylam's failure to achieve a broad-based label for Patisiran. Significantly, several analysts wrote reports describing

a just-released, voluminous FDA Report that contained damning facts about APOLLO III; namely, that Alnylam “does not provide any efficacy data” to the FDA for cardiomyopathy, and that there were “serious safety concerns” over the drug to placebo cardiac death ratio. The FDA report also described at length the Company’s attempts to ameliorate that ratio by re-classifying 2 of the placebo deaths.

75. Alnylam stock again fell over 5% on this adverse news.

DEFENDANTS’ MATERIALLY FALSE AND MISLEADING STATEMENTS

76. Throughout the Class Period, the Defendants made materially false and misleading statements and omissions concerning, among other things: (i) the purported efficacy of Patisiran for the treatment of cardiac symptoms developed as a result of hATTR Amyloidosis; (ii) the purported safety of Patisiran for treating patients suffering from cardiac symptoms developed as a result of hATTR Amyloidosis; (iii) the purported ability of APOLLO III to test the efficacy and safety of Patisiran for patients suffering from cardiac manifestations of hATTR Amyloidosis; and (iv) the potential of Patisiran to obtain a broad-based FDA label that included cardiac manifestations of hATTR Amyloidosis, such as cardiomyopathy, or, at a minimum, a FDA label inclusive of cardiac data from APOLLO III.

September 20, 2017, Alnylam Positive Topline Results from APOLLO III Conference

77. On the first day of the Class Period, September 20, 2017, Alnylam was due to report APOLLO III data. On September 19, 2017, an author for investing publication *SeekingAlpha* discussed the importance of Alnylam’s imminent announcement, writing that “success is critical to the valuation and investor confidence in the platform. A death in the fitusiran program [an Alnylam hemophilia drug] has *brought safety issues to the front of many investors' minds once again*, as this is not the first Alnylam program with safety issues [alluding to Revusiran]. *Alnylam*

(ALNY) needs some good news and its upcoming Phase III APOLLO read-out on patisiran really needs to hit the mark with respect to efficacy and safety.”

78. On September 20, 2017, Alnylam issued a press release titled “Alnylam and Sanofi Report Positive Topline Results from Apollo Phase 3 Study of Patisiran in Hereditary ATTR (hATTR) Amyloidosis Patients with Polyneuropathy,” reporting top line results for APOLLO III, and trumpeting APOLLO III’s success in meeting its primary and secondary endpoints related to polyneuropathy. The press release further stated that it would announce the full data of the study, including cardiomyopathy data in the trial, on November 2, 2017:

[T]he APOLLO Phase 3 study of patisiran, an investigational RNAi therapeutic being developed for patients with hereditary ATTR amyloidosis with polyneuropathy, met its primary efficacy endpoint and all secondary endpoints. The primary endpoint for the study was the change from baseline in the modified neuropathy impairment score (mNIS+7) at 18 months. The key secondary endpoint was improvement in quality of life assessed by the Norfolk Quality of Life Questionnaire-Diabetic Neuropathy (Norfolk QOL-DN)....

The APOLLO trial enrolled 225 hATTR amyloidosis patients with polyneuropathy, representing 39 genotypes, at 44 study sites in 19 countries around the world. Patients were randomized 2:1 to patisiran or placebo, with patisiran administered intravenously at 0.3 mg/kg once every three weeks for 18 months. For both the mNIS+7 and Norfolk QOL-DN endpoint measures provided below, a lower score indicates a better clinical result.

- At 18 months, the mean change from baseline in mNIS+7 was significantly lower in the patisiran group as compared with placebo (p less than 0.00001).
 - The mean and median changes in mNIS+7 impairment scores for patisiran both achieved negative values, indicating an improvement overall and in the majority of patients compared with baseline.
- Patients in the patisiran group experienced improvement in quality of life compared to placebo, as assessed by the Norfolk Quality of Life Questionnaire-Diabetic Neuropathy (Norfolk QOL-DN) (p less than 0.00001).
 - The mean and median changes in QOL scores for patisiran also both achieved negative values, indicating an improvement overall and in the majority of patients compared with baseline.
- All 5 other secondary endpoints also demonstrated statistically significant favorable differences in the patisiran arm compared to placebo (p less than 0.001). These were:
 - NIS-W, the subdomain of mNIS+7 assessing muscle strength;
 - Rasch-built Overall Disability Scale (R-ODS), a patient reported outcome measure of daily living and disability;

- 10-meter walk test, assessing gait speed;
- Modified body mass index (mBMI), assessing nutritional status; and
- COMPASS-31, a questionnaire to assess autonomic symptoms.
- The overall safety profile of patisiran was encouraging.
 - The patisiran and placebo arms had similar frequencies of adverse events (AEs) (96.6 percent and 97.4 percent, respectively) and serious adverse events (SAEs) (36.5 percent and 40.3 percent, respectively).
 - The frequency of deaths in the study was similar in the patisiran (4.7 percent) and placebo (7.8 percent) arms.
 - Patisiran treatment was associated with fewer discontinuations from treatment compared with placebo (7.4 percent and 37.7 percent, respectively) and discontinuations from treatment due to AEs (4.7 percent and 14.3 percent, respectively).
 - AEs reported in greater than 10 percent of patients and seen more frequently with patisiran compared with placebo were peripheral edema (29.7 percent vs. 22.1 percent, respectively) and infusion-related reactions (18.9 percent vs. 9.1 percent, respectively), both of which were generally mild-to-moderate in severity.

Full results, including data from an exploratory analysis of the subgroup of patients with cardiac involvement, will be presented...on November 2, 2017.

79. The same day that Alnylam announced that it had received promising APOLLO III data, it held a conference call with analysts to discuss its findings. During the September 20, 2017 conference call, Defendants discussed the possibility of broadening the intended label for Patisiran beyond polyneuropathy:

Ritu Subhalaksmi Baral [Cowen & Co.]: Congrats as well. Is there anything else—is there anything else you can tell us at this point, just overall on the growth safety of the cardiac subgroup? I know you mentioned it was 57% of the overall study, and there was no imbalance of deaths in the overall study. In fact, there's obviously a separation here in death favoring patisiran. But is that something that you've look[ed] at already?

Akshay K. Vaishnaw [Alnylam]: Yes. The safety by various subsets type of analysis you're alluding to, Ritu, we haven't done as yet. ***But I think looking at the overall safety profile and the fashion in which at least numerically, whilst the numbers are similar, they generally tend to lower numbers for serious adverse events, for deaths, discontinuations, et cetera. For patisiran relative to placebo, it's quite encouraging,*** we think. And if there was a big safety signal, I think we would have seen it in the overall profile.

Defendant Vaishnaw further told analysts that the Company was going to “closely review [the] data, the totality of the data, not just the neuropathy but the cardiomyopathy with them. *And I’m sure we can get an appropriate label by doing that.*”

80. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 drug to placebo cardiac death ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

81. These statements were likewise materially false and misleading when made because Defendant Vaishnaw suggests that the safety profile of Patisiran is encouraging within the context of a broader question concerning the cardiac subgroup, when, in fact, he knew or was reckless in not knowing that there were serious concerns about the safety of the drug due to a high number of cardiac deaths on Patisiran. Given Alnylam’s troubled safety history with clinical trials, Defendant Vaishnaw was acutely tuned into the safety data from APOLLO III.

82. During the conference call, Eliana Rachel Merle, a Credit Suisse analyst asked if, depending on the final analysis of the cardiac subgroup data, another trial might be needed:

I was just wondering if you can give us more color on what kind of education you think is needed to help get doctors to understand the overlap between the neuropathy and cardiac subtypes. And specifically, what are physicians' current level of awareness of this overlap? And then second, well, I know we'll have to wait to see the full cardiac data in November. Is there any thought about running an additional cardiac study to help get a broader label for patisiran? So say, if the regulators ask for more data in the cardiac patients, do [you] think it's worth running another trial in this subtype?

83. Defendant Vaishnaw brushed off the analyst's concern, confident that Alnylam could discuss with regulators how to "incorporate[] [the data] into a label" without a further trial:

Right, right. And I think it'll be interesting to continue and complete our analyses on the cardiac biomarkers, echocardiography and other aspects in the cardiac subgroup in the current study. And that may inform us as to the degree of benefit patients could potentially get from the cardiac aspect with patisiran, and then let's discuss that with regulators on how that may be incorporated into a label. So that's obviously one important aspect.... And I think as we work through the development plans with regulators there, the cardiac aspect and the sort of mixed phenotype that we talk about, are both going to be very important.

84. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 drug to placebo ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

85. During the call, Gena Wang, a Barclays analyst, asked Defendants Maraganore and Vaishnaw what kind of Patisiran label they were seeking:

So just wondering, I think I follow the same line, regarding the cardio subgroup, wondering what is your regulatory strategy for cardio subgroup for the -- for patisiran? Will you try to apply, like for more general ATTR with neuro involvement? And -- with some overlapping with cardio involvement? Or you wanted to apply for specifically for FAP? And similar question for the TTRscO2. Will you have separate trials dedicated only to FAC? Or you would now -- you try to targeting [sic] more general ATTR with certain level of the cardia involvement, try to cover broader patient population?

86. Defendants Maraganore and Vaishnaw both claimed a dual label was eminently possible, in part, because hATTR Amyloidosis should be treated as a single disease with a spectrum of manifestations:

Defendant Maraganore [Alnylam]: Yes. I'm going to have Akshay answer the question. But I'm going to start by just saying that it's very important as the field has evolved now that the field really acknowledges this as one disease with a spectrum of manifestations, neuropathy, cardiomyopathy. So it is a bit antiquated to think of FAP and FAC in terms of the modern understanding of the disease. And that's very relevant to the question you brought forward. So, Akshay, do you want...

Defendant Vaishnaw [Alnylam]: Yes. And consistent with what John just said, if you look at the metrics in APOLLO, 56% of patients were in the cardiac subgroup, but they had existing -- pre-existing cardiac disease at baseline in addition to the neuropathy. And conversely, if you look in our revusiran experience, a significant proportion of patients there also was -- that was so-called cardiomyopathy study had neuropathy at baseline. So those 2 data points underscore, along with work from other sponsors, that this really is a multi-system disease involving a variety of organs, principally nerves and heart. And I think the dataset coming out of APOLLO, which we -- we've just shared the top line results with you today. A lot more diligence ongoing to work through all the other data relating to the cardiac subset. We clearly see improvement in polyneuropathy in the cardiac subset as measured by the mNIS+7 score and other parameters, which is very encouraging for addressing the overall multi-system mixed phenotype. But let's get through the biomark data, the echo data and the other cardiac data. And I think they'll be very informative to give us a data-driven conversation with regulators about the labeling of patisiran with respect to this disease, ATTR amyloidosis, and also the development plan for TTRscO2.

87. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and

omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

88. These statements were also materially false and misleading when made because, despite their assessment that hATTR Amyloidosis should be treated as a single disease with different manifestations, the requirements for obtaining an FDA label included a demonstration of the safety and efficacy of the desired indication, which was not done for cardiac manifestations of the disease in APOLLO III.

89. Presciently, Ritu Subhalaksmi Baral, a Cowen analyst asked on the same conference call whether there was a cardiac death imbalance (the very issue that had sunk the ENDEAVOUR Revusiran trial):

Is there anything else -- is there anything else you can tell us at this point, just overall on the growth safety of the cardiac subgroup? I know, you mentioned it was 57% of the overall study, and there was no imbalance of deaths in the overall study. In fact, there's obviously a separation here in death favoring patisiran. But is that something that you've look at already?

90. Defendant Vaishnaw responded:

Yes. The safety by various subsets type of analysis you're alluding to, Ritu, we haven't done as yet. But I think looking at the overall safety profile and the fashion in which at

least numerically, whilst the numbers are similar, they generally tend to lower numbers for serious adverse events, for deaths, discontinuations, et cetera. For patisiran relative to placebo, it's quite encouraging, we think. And if there was a big safety signal, I think we would have seen it in the overall profile.

91. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

92. Following this conference call, Alnylam's stock skyrocketed from a close of \$75.04 per share on September 19, 2017 to close at \$113.84 per share on September 20, 2017. An increase in stock price of approximately 51%.

November 2, 2017 APOLLO III Results Conference Call

93. On November 2, 2017, on a conference call, the Defendants announced that they had finished fully analyzing the APOLLO III data. With their review complete now, Defendants unequivocally knew or were reckless in not knowing at this time that the 3.5:1 drug to placebo cardiac death ratio posed a serious safety issue that, in addition to the lack of cardiac efficacy data, doomed Alnylam's chances of getting FDA approval of Patisiran for cardiac manifestations of

hATTR Amyloidosis or cardiac data on the drug's label. Yet, Defendant Maraganore still claimed the "safety results [of APOLLO III were] encouraging" – and that the trial showed cardiac efficacy:

Today, we reveal the full breadth of these data, and to our eye, we clearly demonstrate what we believe to be patisiran's transformative potential for patients with hATTR amyloidosis. Specifically, the APOLLO data show[s] highly significant improvements for patisiran in neurological impairment, quality of life, ambulatory ability and activities of daily living, strength and disability and nutritional status as well as *significant improvements in several exploratory cardiac endpoints all at 18 months relative to placebo. We are also encouraged by the tolerability profile shown for patisiran in APOLLO....*

Very importantly, *it also included positive, statistically significant results on a key exploratory cardiac biomarker and echocardiographic endpoints in the cardiac subpopulation.* Importantly, the favorable effects measured by these neuropathy and cardiac endpoints led to functional improvements shown through, for example, patient's ambulatory ability measured with a 10-meter walk test. Overall, we believe these Phase III results are robust with strikingly low p-values and consistency across all baseline characteristics evaluated. *Moreover, the safety results are encouraging.*

94. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

95. Following Defendant Maraganore's comments, Defendant Vaishnaw touted the exploratory cardiac endpoint data yielded from APOLLO III as if that was sufficient to obtain FDA approval for a broader-based label for Patisiran:

Now an important part of the APOLLO study was to assess the effects of patisiran on cardiac manifestations of hATTR amyloidosis as this is a very common and often the deadliest feature of the disease. As a reminder, the cardiac subpopulation was prespecified and comprised of about 56% of the entire APOLLO population. About 47% of placebo patients were in the cardiac subpopulation, while about 61% of patisiran patients were in this group. We focused our exploratory assessment on a number of biomarker and echo parameters in the subpopulation. *We're very pleased to report that patisiran treatment was associated with statistically significant improvements in certain key exploratory cardiac endpoints at 18 months.* Specifically, there was a significant reduction, i.e. improvement in NT-proBNP levels in patisiran patients compared to an increase or worsening in the placebo group. The median treatment difference between the 2 groups was 370.2 mcg per mL, and this was a highly significant difference with a nominal p-value of 7.74 times 10 to the power of -8 based on analysis of law of transformed values. It's encouraging to see favorable effects of patisiran on NT-proBNP, which is associated with survival in the closely related disease of AL cardiac amyloidosis and also with positive changes in heart structure and function.

Turning to echo endpoints. Significant improvements in left ventricular wall thickness and longitudinal strain were observed in patisiran patients relative to placebo. With LV wall thickness, there was a mean 0.93 (sic) [0.093] millimeter improvement associated with patisiran treatment. And with longitudinal strain, there was a mean absolute 1.37% improvement. These changes are statistically significant and also meaningful.

Finally, as a surrogate for functional improvement, there was a significant improvement in 10-meter walk test in the patisiran cardiac subpopulation relative to placebo with a 0.35 meter per second treatment benefit. Changes relative to baseline were also measured for troponin, LV mass, LV ejection fraction but did not reach statistical significance at the 18-month time point.

There were also clinically meaningful differences in a number of other exploratory endpoints, such as small and large nerve fiber function, grip strength, PND stage and the EQ-5D assessment of quality-of-life measure. We look forward to presenting those and other data at future meetings. But they also speak to the point John made earlier about the broad effects of TTR knockdown with patisiran toward many manifestations of this multisystem disease.

96. Defendant Vaishnaw then falsely represented that Patisiran was likewise safe for the cardiac subgroup based on APOLLO III data:

So with that, let's now turn to the safety results, starting on Slide 24. Patisiran showed an encouraging safety and tolerability profile relative to placebo with up to 18 months of dosing. Specifically, the overall incidence of adverse events, severe adverse events, serious adverse events were all similar between patisiran and placebo arms....

* * *

Let's now touch on safety in the cardiac subpopulation with a focus on cardiac AEs. The overall frequency of SAEs (sic) [AEs] was numerically lower in the patisiran arm of the cardiac subgroup, and there was no signal with regard to arrhythmias based on examination of reported AEs. In fact, these were also numerically lower in the patisiran arm. You'll also see that the frequency of deaths was 11.1% on placebo and 5.6% on patisiran in the cardiac subpopulation.

97. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

98. Once the question and answer portion of the conference call started, Terence C. Flynn, a Goldman Sachs analyst immediately asked about Alnylam's confidence as to whether it would receive a dual or "broad" label for Patisiran:

Maybe just one for the company. First, maybe Akshay, you could speak to your confidence in obtaining a broad label that would allow you to treat the mixed

phenotype patients. And then for Dr. Hawkins, just wondering how you'd plan to employ patisiran relative to inotersen based on the data that you saw today. And would you use either of these drugs in the mixed phenotype patients, assuming it's reimbursed?

99. In response, Defendant Vaishnaw claimed he was confident based on APOLLO

III that Alnylam would indeed get a broad-based label for Patisiran:

Yes. Sure. I think looking at the data and seeing the rather comprehensive nature of the effects of the drug on virtually every dimension of the disease we've looked at, I think we can confidently build data-driven arguments to regulators to say we see impact on sensory, motor, autonomic, gut, bladder and cardiac aspects of the disease. *And as such, we think that should be all incorporated into the label, and we're hoping that those data-driven arguments lead to the broad indication that seems justifiable. But ultimately, of course, they have to adjudicate on that. But I think we're confident we can make strong arguments.*

100. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

101. These statements were also materially false and misleading when made because Defendant Vaishnaw knew or was reckless in not knowing that, despite Alnylam's assessment that hATTR Amyloidosis should be treated as a single disease with different manifestations, the

requirements for obtaining an FDA label included a demonstration of the safety and efficacy for each desired indication of the drug, which was not done for cardiac manifestations of hATTR Amyloidosis in APOLLO III, and, as such, would require a completely separate study by Alnylam.

November 7, 2017 Alnylam Earnings Call

102. On November 7, 2017, Alnylam held another conference call with analysts. On that call, Defendant Vaishnaw continued to claim Patisiran showed cardiac efficacy and safety in APOLLO III:

We also reported favorable and significant changes in several exploratory cardiac measures in patisiran-treated patients in the prespecified cardiac subpopulation. These included NT-proBNP, certain echocardiographic parameters and the 10-meter walk time. Notably, with NT-proBNP there was a median 49.9 pg/ml decrease or improvement in the patisiran arm compared with a 320 pg/ml increase or worsening in the placebo arm. This over 300 pg/ml difference between patisiran and placebo is considered a clinically meaningful difference. Similarly, the effects on left ventricular wall thickening and longitudinal strain are also clinically meaningful. Of note, these changes in biomarker and echocardiographic measures also associated with an improvement in functional status, as documented with the 10-meter walk time. Here, patients in the cardiac subpopulation had a statistically significant and clinical meaningful 0.35-meter per second improvement in this measure. Changes relative to baseline were also measured for troponin I, LV mass and LV ejection fraction were not statistically significant at the 18 point -- 18-month time frame. *So overall, for a majority of patients, we are seeing reversal of disease progression and improvement in their disease symptoms.*

* * *

On the safety side, patisiran showed an encouraging safety and tolerability profile relative to placebo with up to 18 months of dosing. The most commonly reported adverse events that occurred more frequently in patisiran-treated patients were generally mild to moderate and included peripheral edema and infusion-related reactions. *The frequency of death and serious adverse events was similar in the patisiran and placebo groups, with respect to infrequency of events being consistent with the underlying disease, hATTR amyloidosis.* There were no safety signals related for steroid premed regimen and also no signals with regard to thrombocytopenia, hepatic or renal dysfunction. *Patisiran also showed an encouraging safety and tolerability profile in the cardiac subpopulation.* With

99% of eligible patients now enrolled into the global OLE study, we look forward to generating longer-term results for patisiran on safety and efficacy.

* * *

One thing that I could just add is that for the current generation of molecules like tafamidis and diflunisal, we know from our experience with the patisiran Phase II open-label extension study, that certainly, the combination there didn't provide any great benefit over patisiran alone, and I think that, along with the observations of patisiran as monotherapy, which we revealed in last week's show, ***really, the great potential of this drug to be of service to the vast majority of patients with a wide spectrum of disease, with polyneuropathy and significant cardiomyopathy.***

103. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

104. These statements were also materially false and misleading when made because, despite Alnylam's assessment that hATTR Amyloidosis should be treated as a single disease with different manifestations, the requirements for obtaining an FDA label included a demonstration of the safety and efficacy for each desired indication of the drug, which was not done for cardiac

manifestations of hATTR Amyloidosis in APOLLO III, and, as such, would require a completely separate study by Alnylam.

November 29, 2017, Piper Jaffray Healthcare Conference

105. On November 29, 2017, Defendant Maraganore participated in the Piper Healthcare Conference on behalf of Alnylam. At that conference, Piper Jaffray Research Analyst Edward Andrew Tenthoff asked Defendant Maraganore for some clarification concerning the “blurred” lines created by Defendants’ prior statements concerning Patisiran’s potential for getting a broad-based FDA label for the treatment of polyneuropathy and cardiomyopathy manifestations of hATTR Amyloidosis:

So let me ask you a quick follow-up on that. Do you expect it to be in that (inaudible) Adcom, especially with Ionis' drug kind of filing right around the same time since this is the novel approach a new disease. And I want to tease out a little bit more about what you're talking about on the cardiac side, because while the study really was enrolled primarily polyneuropathy patients, sort of the lines have really blurred with traders. So tell us a little bit about kind of what you think the ultimate label...

106. Because it aided Alnylam’s narrative of imminent FDA approval of one drug to treat both hATTR manifestations, Defendant Maraganore purposefully left the issue blurry and emphasized that a broad-based label for Patisiran was indeed very possible:

So as it relates to the label, obviously, it's too soon to say for sure, but we believe the data really pointed an impact of patisiran across the entirety of the disease. And we really believe that the cardiac results that we showed in addition to the effects on neuropathy, but also if you look at the adverse event profile of patisiran, which really compares very favorably with placebo, you can begin to tease out an effect of patisiran against the whole range of other manifestations of the disease, renal features, autonomic disease, gastrointestinal disease features. And we see an impact of patisiran on things like falls, syncope, anemia, features of amyloid deposition, not just in the heart and the nerves, but also in the gut and other tissues and the kidneys. So we're -- we think there really is a broad effect of patisiran in the disease, and we think that, that bodes well for conversations we'll have with the FDA around a broader label for the product.

107. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

108. These statements were also materially false and misleading when made because, despite Alnylam's assessment that hATTR Amyloidosis should be treated as a single disease with different manifestations, the requirements for obtaining an FDA label included a demonstration of the safety and efficacy for each desired indication of the drug, which was not done for cardiac manifestations of hATTR Amyloidosis in APOLLO III, and, as such, would require a completely separate study by Alnylam.

December 14, 2017, BMO Capital Markets Prescriptions for Success Healthcare Conference

109. On December 14, 2017, Alnylam presented at the BMO Capital Markets Prescriptions for Success Healthcare Conference. At the conference, Defendant Greenstreet discussed the purported merits of Patisiran, including its merits for cardiac patients based on APOLLO III, at great length:

And the data that we delivered was pretty overwhelming from an efficacy and very impressive from a safety perspective as well, where with the primary endpoint we were able to demonstrate and deliver 34 points difference between placebo and patisiran. And actually it was even more remarkable with a negative 6 change from baseline. And that means that patients were actually improving with treatments with patisiran. And this is pretty impressive result for a condition where you generally don't see reversal of disease. And I think, kind of, one of the things that really struck me about that dataset was the fact that it demonstrated the potential for future and also lead to halt progression of disease, this will actually reverse disease.

The other striking feature for me of the data was just how consistent the efficacy was across all the parameters that we looked at, the primary endpoints and at least to the whole range of secondary endpoints. And all of them pointed towards significant efficacy for patisiran. It's not often you get a dataset where everything's so internally consistent. It's ultimately the kind of second most impressive aspect of the data. ***The third was actually around the safety. And again, what we saw was that the safety profile actually looked more better in patients being treated with patisiran than those receiving placebo. And again, that's quite a remarkable result that you actually get better safety profile with drug than with placebo.*** So I think, in general, what I would kind of summarize the data by saying is, I've been in the drug development space for about 25 years, and actually it's one of the most impressive datasets that I have ever seen. The data also is very consistent across all the different demographics, race, age, gender, geography. ***And you may be aware, over half of the patients had cardiac manifestations of the disease. And in those patients, we not only saw improvements in neurological endpoints, like the mNIS, but we also saw some very encouraging data around the cardiac endpoints, so biomarkers, so NT-proBNP, echocardiographic features in terms of ventricle wall thickness and strain. And importantly, functional parameters. So improvements in the 10-meter walk test.*** So really, if you look across the whole dataset, it's really quite remarkable result.

110. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and

conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

111. These statements were also materially false and misleading when made because, despite Alnylam's assessment that hATTR Amyloidosis should be treated as a single disease with different manifestations, the requirements for obtaining an FDA label included a demonstration of the safety and efficacy for each desired indication of the drug, which was not done for cardiac manifestations of hATTR Amyloidosis in APOLLO III, and, as such, would require a completely separate study by Alnylam.

January 7, 2018, Conference Call to Discuss Sanofi Alliance Restructuring

112. On January 7, 2018, Defendants held a conference call to discuss the restructuring of Alnylam's alliance with Sanofi. On that call, a Barclays analyst asked Defendants Maraganore and Vaishnaw to "share a little bit more regarding the potential risk through from Pfizer trial [for competing drug Tafamidis]? And also regarding the specific timing, like when would you do that and like how long do you expect the trial to read out, especially the primary endpoint thinking?"

113. In response, Defendants Maraganore and Vaishnaw touted Patisiran over Pfizer's Tafamidis, which was intended to treat hATTR Amyloidosis patients with cardiomyopathy, in relevant part, as follows:

Defendant Maraganore [Alnylam]: Yes, yes, that's a really good question that Akshay should comment on. I'll just say that, obviously, Pfizer with tafamidis has conducted a trial that we do expect to read out sometime in the first half of the year in both hereditary ATTR with cardiomyopathy and also with wild-type ATTR. So Akshay, how does that factor into our thinking?

Defendant Vaishnaw [Alnylam]: Yes, the major point for me is considering the stabilizers like tafamidis and diflunisal and what is understood at this point in time about how they've performed that help patients in neuropathy and cardiomyopathy settings, most patients of course have mixed phenotype of hATTR amyloidosis. The effects are modest. And as we note, tafamidis wasn't approved in the United States. It was approved under special circumstances in the EU. There's a significant literature already accumulated showing progression on tafamidis. So I think with patisiran, we've understood that TTR knockdown, actually getting rid of the bad proteins, the pathogenic proteins, allows for improvement in disease in the majority of patients, and that's a really important observation. And I think if the Pfizer ATTRact study hits its endpoint, we would only be encouraged that TTR knockdown should yield yet better results with our compounds in that setting. And so we would be greatly encouraged, and I think it's great news for patients to have additional agents at play.

114. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

115. These statements were also materially false and misleading when made because, despite Alnylam's assessment that hATTR Amyloidosis should be treated as a single disease with different manifestations, the requirements for obtaining an FDA label included a demonstration of the safety and efficacy for each desired indication of the drug, which was not done for cardiac

manifestations of hATTR Amyloidosis in APOLLO III, and, as such, would require a completely separate study by Alnylam.

January 8, 2018, JPMorgan Healthcare Conference

116. On January 8, 2018, Defendants Maraganore, Greene, Vaishnaw, and Greenstreet participated in a Healthcare Conference hosted by JP Morgan.

117. In introductory remarks, Defendant Maraganore once again continued to tout Patisiran's cardiac efficacy and safety based on APOLLO III, as well as the drug's potential for obtaining a broad-based FDA label, in relevant part, as follows:

Now in addition to the neurological impact that we saw with patisiran, we also looked with great interest at the effects of patisiran on the cardiac endpoints in the study. And in this regard, we had a prespecified cardiac subpopulation that included about 56% of the total study. In this cardiac subpopulation, we were very pleased to see that patisiran showed a significant reduction in NT-proBNP levels. This is a biomarker of cardiomyopathy that is known to -- it is associated with survival in a number of heart failure settings. We also showed evidence for cardiac remodeling by looking at echocardiographic changes in the heart of these patients. And here, we showed about a 1 millimeter decrease in leftventricular wall thickness and a significant improvement, or stabilization in this case, of longitudinal strain. These benefits on NT-proBNP and echocardiographic measures, in turn, were demonstrated on functional measures, specifically gait speed. Gait speed is often referred to as the sixth vital sign and is highly correlated with survival. And in this study, we were able to demonstrate that patients receiving patisiran had a stabilization in their gait speed compared to a significant decrease in gait speed for those patients receiving placebo.

These cardiac data, in addition to the neurological data, truly demonstrate the transformational potential of patisiran that was evidenced in the APOLLO study. Let's now turn to safety. We were very pleased with the safety results from APOLLO. The majority of adverse events were mild to moderate in severity. The 2 adverse events that occurred most frequently with patisiran were infusion-related reactions and peripheral edema. These were mild to moderate. They decreased over time in this study, and they led to only one study discontinuation. If you look overall at the adverse event profile and if you focus on the right-hand side of the slide, specifically at the table, you'll actually note that the incidence of adverse events leading to either discontinuations or withdrawals was lower in the patisiran arm compared to placebo. And while we can characterize the mortality rate as being

similar between drug and placebo, it's actually numerically lower in the patisiran arm both in the overall study population but also in the cardiac subpopulation as well. Very importantly, we saw no evidence of a safety signal related to thrombocytopenia or renal toxicity, which has been described in other agents in development in this space.

Now when we take a step back and look at the totality of the data from APOLLO, what's impressive to us is whether we look at neurological endpoint data, autonomic disease data or cardiac disease data, we're seeing an impact of patisiran across the whole spectrum of this disease. And frankly, that makes a lot of sense because we're dealing with a disease that is produced, that is caused by a production of mutant wild-type TTR in the liver, and we have a drug, patisiran, that is very effective at lowering TTR levels in the liver. So it is not -- it should come as no surprise, in fact, that patisiran has a broad-based effect across the whole spectrum of this disease. And for those reasons, we are seeking an approval for patisiran with a broad label namely for the treatment of hATTR amyloidosis, and we look forward to working with regulators around that label.

118. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

119. These statements were also materially false and misleading when made because, despite Alnylam's assessment that hATTR Amyloidosis should be treated as a single disease with

different manifestations, the requirements for obtaining an FDA label included a demonstration of the safety and efficacy for each desired indication of the drug, which was not done for cardiac manifestations of hATTR Amyloidosis in APOLLO III, and, as such, would require a completely separate study by Alnylam.

120. Following these comments, an unidentified analyst asked Defendant Maraganore: “John, as far as the cardiac data and how that might wind up in the label, can you sort of just outline what you think the scenarios are, the possible outcomes are? And then when do you think you’ll get—start to get some more clarity from the FDA on that?”

121. Defendant Maraganore confidently responded that the data “support[ed] the broadest of all the labels” and Defendant Vaishnaw added that he likewise was confident that Alnylam would get cardiac data on the Patisiran label:

Defendant Maraganore [Alnylam]: Yes. Well, [Wayne] -- so [Wayne's] question is when -- what are the different scenarios for cardiac data in the label, and then how do we get -- when do we get clarity on that from the FDA? Let me -- can I take a crack and then...

Defendant Vaishnaw [Alnylam]: Sure.

Defendant Maraganore [Alnylam]: Okay. Let's try it this way. So we've asked for hATTR amyloidosis as the indication statement for patisiran, and we think the data supports that. And we are very happy to have a dialogue and we'll have a dialogue with the FDA around that label. I think that if you look at the spectrum, that's a win, that's our ask that we think is supported by the data. The other extreme might be limited to polyneuropathy patients, okay? And then the question is, do we or do we not, in the label itself, have our cardiac endpoint data within the label? And the reason that's relevant is it helps on the promotional efforts for how we can approach cardiologists and so forth with our data set. Now regardless of all that, at the one extreme, and if you will, the more narrow extreme, hATTR with polyneuropathy, well, that still addresses the mixed phenotype patient population. Patients that have cardiomyopathy that happen to have neuropathy would benefit -- we know, would benefit from patisiran. And so we do still capture a broad swath of the disease population from a promotional perspective. But obviously, we do believe the data support the broadest of all the labels, and that's what we've submitted with FDA and EMA. I mean, do you have anything to add? Did I handle that okay?

Defendant Vaishnaw [Alnylam]: Very well. Yes, I think we and others, as we've studied this disease, have really laid out the fact that the vast majority of patients with a mutation in the TTR gene have elements of the neuropathy and cardiomyopathy. And whilst in our Phase III study in APOLLO, just over half were prespecified to be in a cardiac subgroup, patients well beyond that had cardiac involvement, okay? ***So what John is saying is that this sort of passing between the neuropathy and cardiomyopathy, as long as we get some element of data from the cardiac endpoints of the label, which we're confident will occur because of the meaningfulness of those data, and I think the agency is sympathetic to the needs of prescribers that they need to convey to patients what benefit they can expect from the drug.*** And if those kinds of data aren't in there, then they can't fully help the patient understand why they're being given the drug. ***So I think regardless, ultimately, of whether we get a very broad label or not, with the inclusion of some of those cardiac data in there and the very fact that the disease is a mixed phenotype, we can help the vast majority of patients here with patisiran.***

122. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

123. These statements were also materially false and misleading when made because, despite Alnylam's assessment that hATTR Amyloidosis should be treated as a single disease with different manifestations, the requirements for obtaining an FDA label included a demonstration of the safety and efficacy for each desired indication of the drug, which was not done for cardiac

manifestations of hATTR Amyloidosis in APOLLO III, and, as such, would require a completely separate study by Alnylam.

Alnylam Form 10-K

124. On February 15, 2018, Alnylam filed a Form 10-K for fiscal year 2017 with the SEC (“2017 10-K”), which was signed and certified by Defendants Maraganore and Soni. In regards to APOLLO III, the 2017 10-K provided, in relevant part, that:

Cardiac Subpopulation Results: Favorable and significant changes in several exploratory cardiac measures, including N-terminal pro b-type natriuretic peptide, or NT-proBNP, and certain echocardiographic parameters, were reported in patisiran-treated patients with pre-defined cardiac involvement (baseline left ventricular (LV) wall thickness ≥ 1.3 cm with no history of hypertension or aortic valve disease). Specifically:

- Patisiran treatment resulted in a median decrease (improvement) of 49.9 pg/ml in NT-proBNP levels as compared to a median increase (worsening) of 320 pg/ml reported for the placebo arm at 18 months (nominal $p=7.74 \times 10^{-8}$, based on analysis of log-transformed values).
- Regarding echocardiographic measures, patisiran treatment resulted in a mean 0.93 mm reduction (improvement) in left ventricular (LV) wall thickness (nominal $p=0.0173$) and a mean absolute 1.37 percent improvement in longitudinal strain (nominal $p=0.0154$) relative to placebo.

Safety and Tolerability: ***Patisiran showed an encouraging safety and tolerability profile relative to placebo with up to 18 months of dosing.*** Specifically:

- The most commonly reported adverse events, or AEs, that occurred more frequently in patisiran patients were peripheral edema (29.7 percent versus 22.1 percent in placebo) and infusion-related reactions, or IRRs (18.9 percent versus 9.1 percent in placebo). These were generally mild to moderate in severity and only one patient discontinued due to an IRR (0.7 percent).
- Compared to placebo, patisiran treatment was associated with fewer treatment discontinuations (4.7 versus 14.3 percent) and fewer study withdrawals (4.7 versus 11.7 percent) due to AEs.
- The incidence of serious adverse events, or SAEs, across the patisiran (36.5 percent) and placebo (40.3 percent) groups was similar.
- SAEs reported in 2 or more patients in the patisiran group included: diarrhea (5.4 percent), cardiac failure, congestive cardiac failure, orthostatic

hypotension, pneumonia, and atrioventricular block complete (2 percent each). These were all considered unrelated to patisiran, except for one SAE of diarrhea. SAEs occurred with similar frequency in the placebo group, except for diarrhea (1.3 percent in placebo group).

- ***Deaths were recorded with a similar incidence across the patisiran (4.7 percent) and placebo (7.8 percent) treatment groups.***
 - No deaths were considered related to study drug.
- There were no safety signals with regard to hepatic or renal function, or evidence of thrombocytopenia, due to patisiran.

125. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

126. In particular, while deaths may have been “recorded with a similar incidence across the patisiran (4.7 percent) and placebo (7.8 percent) treatment groups[,]” this statement was materially misleading because it omitted to disclose that cardiac deaths were recorded with a *significantly dissimilar incidence* for Patisiran and placebo.

127. Defendants Maraganore and Soni were responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rule 13a-15(e) and

15(d)-15(3)) pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. Defendants Maraganore and Soni both signed certifications that the 2017 10-K did not contain any untrue statement of material fact or omit to state a material fact. They also certified that they designed disclosure controls and procedures and that they evaluated the effectiveness of such controls. Defendants also stated in the 2017 10-K that the Company evaluated the effectiveness of its disclosure controls and procedures and based on its evaluation, Defendants Maraganore and Soni concluded that the Company's disclosure controls and procedures were effective as of February 15, 2018. The Company's management also concluded that its internal control over financial reporting was effective as of February 15, 2018.

128. Alnylam filed similar certifications in its Form 10-Qs throughout the Class Period. Each of these certifications were materially false misleading when made because the SEC filings alleged to be misleading herein omitted to state material facts concerning the safety and efficacy of Patisiran to treat cardiac patients suffering from hATTR Amyloidosis based on APOLLO III.

February 8, 2018, Q4 2017 Earnings Call

129. On February 8, 2018, Alnylam hosted an earnings call to discuss the Company's fourth quarter 2017 and year-end earnings. Defendants Maraganore, Greene, Soni, and Greenstreet participated in the call.

130. During the call, Defendant Maraganore once again claimed that the APOLLO III results "support[ed] a broad label" for Patisiran that would include cardiac data:

We also received a number of important regulatory designations for patisiran, including break-through therapy, priority review status as well as an expanded orphan drug designation for ATTR amyloidosis, all by the FDA, and then, accelerated assessment by the EMA and promising innovative medicine designation by the UK's MHRA.

We believe that all of these regulatory accolades reflect a very promising profile of patisiran seen in APOLLO and a very high unmet need in hATTR amyloidosis

patients. The review process is now fully underway and we announced last week that we have a PDUFA date of August 11, although we expect an expedited review that could lead to an earlier approval. We believe the APOLLO results highlight the potential impact of patisiran across the full spectrum of hATTR amyloidosis disease, and we believe that the results support a broad label for the product. Assuming regulatory approvals, we remain on track for commercial launch in the U.S. in mid-2018 and in Europe in late 2018.

131. Later in the call, Vincent Chen, a Sanford C. Bernstein analyst, asked Defendants Maraganore and Vaishnaw about the likelihood of a broad-based label for Patisiran that would include cardiac data from APOLLO III:

I was wondering if you could provide some color on how you're thinking about the likelihood of a broad label for patisiran. I guess both you and I know it's submitted for a broad label since -- do we know of advisory committee's plan? So regulators clearly think they have a view on the likely label, whether it ends indeed broader in (inaudible) the only. I guess, two parts to the question, one, is it fair to say that the breadth of the label really hinges on how robustly regulators view cardiac substudy data, for example, prespecified, robust mutual endpoint? And two, if so, what is your sense from your discussions with the regulators themselves and also with your regulatory consultants with respect to how the FDA is likely to view the robustness/efficiency of the cardiac substudy and the implications for the label?

132. Defendants Vaishnaw and Maraganore responded as follows:

Defendant Maraganore: Okay. Those are great questions. Akshay, do you want to tackle them?

Defendant Vaishnaw: Yes. Vincent, I mean, we're obviously very hopeful that we can achieve a broad label based on just how comprehensive the data in APOLLO were speaking to all dimensions of the disease, and by that I mean the peripheral neuropathy, the autonomic neuropathy, the cardiac outcomes and all of that then supported by changes in very important secondary measures like Quality of Life, body mass, activities of daily living, et cetera. So -- and I think that is all going to be looked at very carefully by regulators. Equally, they'll want to -- I imagine, if you're convinced that the input population that was studied in APOLLO is truly representative of the breadth of what is hATTR amyloidosis. We certainly believe it is. As you know, over 50% of patients had significant cardiomyopathy as well as the neuropathy, and we believe that we have very nicely tested the hypothesis of TTR reduction and its impact on the full breadth of the disease. The cardiac data themselves will, of course, be very important, and I think the internal consistency

of all the data will be important. So we've got to elaborate (inaudible) to work through all that stuff, of course. And I think that we're optimistic, but let's see where they end up.

Defendant Maraganore [Alnylam]: Yes, I would agree with that. And obviously, I think it goes without saying that APOLLO -- ***the APOLLO data being as robust as they were and as amazingly consistent across all aspects of the disease is the key point here.***

133. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

134. These statements were also materially false and misleading when made because, despite Alnylam's assessment that hATTR Amyloidosis should be treated as a single disease with different manifestations, the requirements for obtaining an FDA label included a demonstration of the safety and efficacy for each desired indication of the drug, which was not done for cardiac manifestations of hATTR Amyloidosis in APOLLO III, and, as such, would require a completely separate study by Alnylam.

135. The Sanford C. Bernstein analyst then asked a key question: “Would it *matter at all that there wasn't a primary endpoint focused on sort of cardiac* and that the primary was much more focused on the neuropathy? And is there a world where it would be potentially a shorter study just saying, let's redo a cardiac population with the primary really focused specifically on around the cardiac endpoints?”

136. In response, Defendant Vaishnaw claimed that the lack of a primary cardiac endpoint in APOLLO III simply was “not the issue”, downplaying any remote concern that the efficacy of Patisiran to treat cardiac patients was supported by APOLLO III and thus the drug therefore might not obtain a broad-based label on that basis:

I think there are aspects to your questions which, obviously, we should allow regulators ultimately to answer. But from our perspective, what I would say is that the issue with the label is that you want to inform prescribers and those that will receive the drug, what is the capacity of this drug in terms of the efficacy can confer and what is the -- what are the potential issues with safety. That's what we want to do with the label. *We feel, and I think most people will agree with, that the fact that the cardiac outcomes weren't the primary endpoint is not the issue here.*

137. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the

3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

138. These statements were also materially false and misleading when made because, despite Alnylam's assessment that hATTR Amyloidosis should be treated as a single disease with different manifestations, the requirements for obtaining an FDA label included a demonstration of the safety and efficacy for each desired indication of the drug, which was not done for cardiac manifestations of hATTR Amyloidosis in APOLLO III, and, as such, would require a completely separate study by Alnylam.

February 12, 2018 BIO CEO and Investor Conference

139. On February 12, 2018, Defendant Maraganore attended the BIO CEO and Investor Conference as a representative of Alnylam. During that conference, Defendant Maraganore again trumpeted Patisiran's ability to show efficacy for cardiac patients based on APOLLO III:

Now when we look at the entirety of the data from the APOLLO study, what's impressive to us is that we're *seeing a consistent effect across a number of primary and secondary endpoint measures* that really measure the sensorimotor, autonomic nervous system dysfunction, *but also the cardiac impairment that occurs in these patients*. And then also, if we even look at the adverse events that were reported in the study, which were lower in the drug arm compared to the placebo arm, these *show also that patisiran is having a very complete effect on the progression of this disease by halting and, in fact, reversing disease progression*. So for these reasons, we're encouraged by the type of data that we've generated, and we've submitted our NDA and EMA -- MAA to the FDA and EMA, respectively, with a goal of getting a broad label for patisiran for the treatment of ATTR amyloidosis.

140. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac

efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

141. These statements were also materially false and misleading when made because, despite Alnylam's assessment that hATTR Amyloidosis should be treated as a single disease with different manifestations, the requirements for obtaining an FDA label included a demonstration of the safety and efficacy for each desired indication of the drug, which was not done for cardiac manifestations of hATTR Amyloidosis in APOLLO III, and, as such, would require a completely separate study by Alnylam.

February 15, 2018 Leerink Partners Global Healthcare Conference

142. On February 15, 2018, Defendant Greene participated in the Leerink Global Healthcare Conference on behalf of Alnylam.

143. During that conference, Paul Andrew Matteis, a Leerink Partners analyst, asked Defendant Greene about the likelihood of Patisiran obtaining a broad-based label that would include cardiac data from APOLLO III: "Let's start with patisiran. Alnylam has talked about the expectation of a broad hATTR label. Is this based off any discussions with the FDA? And what data are you conveying to the FDA to make your case?"

144. Defendant Greene claimed Alnylam “anticipate[d] a broad label” – at the very least “all of the [cardiac] data” on the label – and even claimed that the cardiac safety profile of Patisiran further supported the broad label:

Yes, when we look at the APOLLO results, and those were presented at EC-ATTR in Paris just a couple months ago, 2 things really became very clear to the entire congress. And it really started to change everybody's view of hereditary ATTR amyloidosis. Number one is it became pretty clear that hereditary amyloidosis is, in fact, one disease. Now there's a spectrum of manifestations of the disease from polyneuropathy, autonomic dysfunction and cardiomyopathy, but it became pretty clear that it's one continuum of disease, not different than what was believed even 3 years or 4 years ago, that these were disparate disease of poly and cardiomyopathy, so one disease. The second thing that became clear based upon the APOLLO results is that patisiran has beneficial impact across the broad spectrum of the disease. As you know, on mNIS+7, the primary endpoint, a majority of patients actually improved in their neurological impairment, which is a remarkable and unexpected result for a progressive, debilitating, fatal disease. To see reversal of the disease is pretty spectacular. And likewise, we saw, even for the prespecified cardiac subgroup, an improvement in that subgroup as well. For example, the treated patients on patisiran had twice the improvement in ambulatory ability than placebo had, where they all got worse. And then of course, biomarkers like proBNP also improved, that matches that ambulation. So in the neurological impairment, the autonomic impairment, gut dysfunction, diarrhea as well as the cardiac involvement, we saw beneficial effects of patisiran broadly. And when you step back and look at even the safety profile, it was very interesting that the drug and placebo arm were about the same, if not favoring drug in terms of overall safety profile. So it's pretty clear that patisiran can impact the treatment of hereditary ATTR amyloidosis. And because of those data and some of the interactions with key opinion leaders and others, we believe that a broad label is warranted. Now of course, we have to get into the detailed label discussions with the agency. ***But we anticipate a broad label. We anticipate having, at least in the clinical section, all of the data I just described, that gives us the ability to educate physicians on the potential beneficial impact that patisiran can have on the hereditary ATTR amyloidosis patients.***

145. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO

III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

146. These statements were also materially false and misleading when made because, despite Alnylam's assessment that hATTR Amyloidosis should be treated as a single disease with different manifestations, the requirements for obtaining an FDA label included a demonstration of the safety and efficacy for each desired indication of the drug, which was not done for cardiac manifestations of hATTR Amyloidosis in APOLLO III, and, as such, would require a completely separate study by Alnylam.

147. In response to Defendant Greene's answer, Matteis asked a follow-up question concerning whether the FDA might only allow Patisiran for milder forms of cardiomyopathy:

Okay. It's interesting, a comment that Akshay made on your call made me wonder if there's a mid-case. And so he commented that the APOLLO population is generally consistent with the broader population of hATTR and that, that's what matters to the FDA, right, is the study consistent with the label population? But the study itself excluded patients with Class III and Class IV heart failure, which seems to kind of include – exclude more the serious [cardiomyopathy] patients. Is there - - do you think there's a scenario where the FDA splits the difference and kind of only indicates patisiran for the milder forms of cardiac disease?

148. Defendant Greene doubled down in his response, claiming Alnylam “anticipated” a broad label based on APOLLO III that included cardiac data, “period, full stop”:

That's not what we anticipate. We anticipate a label that patisiran will be indicated for the treatment of hereditary ATTR amyloidosis, period, full stop. It's possible that there can be statements about not studied in. Those things can always come up in labels. I think commercially, it doesn't really matter if that's specified. What our key to success will be finding patients in earlier diagnosis. So the Stage 3 and 4 heart failure patients that exist today, quite frankly, we hope, don't exist in 5 or 6 years, because we're able to earlier diagnose. And a patient gets to a Stage 3 and 4 often because they've been popping around the health care system for a decade and misdiagnosed and actually being given drugs, like beta blockers or others, that are detrimental to the disease, not beneficial. So if we get the education right, cardiologists will be looking for this disease much earlier, and we'll be finding patients earlier.

149. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

150. These statements were also materially false and misleading when made because, despite Alnylam's assessment that hATTR Amyloidosis should be treated as a single disease with different manifestations, the requirements for obtaining an FDA label included a demonstration of the safety and efficacy for each desired indication of the drug, which was not done for cardiac

manifestations of hATTR Amyloidosis in APOLLO III, and, as such, would require a completely separate study by Alnylam.

March 13, 2018 Cowen Healthcare Conference

151. On March 13, 2018, Defendants Vaishnaw and Maraganore, on behalf of Alnylam, participated in the Cowen Healthcare Conference. At that conference, a Cowen and Company analyst asked about the Patisiran label as follows:

[D]oesn't the FDA need to discuss the potential for the mixed phenotype simplifications for the label or what is the agency's understanding of this spectrum of disease running from the neuro path to the cardiomyopathy?

152. Defendant Vaishnaw once again emphasized that the endpoint structure was “comprehensive” for APOLLO III, and that the lack of a cardiac endpoint was not a problem for obtaining a broad-based label for Patisiran. Defendant Vaishnaw’s response implied that regardless of the endpoint listed, APOLLO III’s data supported the efficacy of Patisiran for cardiac patients:

Well, the agency a couple of years back have done a very substantial amyloidosis meeting with patient groups and with academics interested in the disease to understand the disease fully. And so they are well acquainted with the disease and the full spectrum of its impact on the neurological system and the cardiac system. ***In addition to that, we designed patisiran in a way to ensure that we maximally capture impact on both neurological and cardiac aspects, and if you look at the endpoint structure, in APOLLO, which we have shared at other meetings, we certainly think that we have done a comprehensive job addressing that.*** And so we have aspects on the neurological outcome, in terms of (inaudible) plus some endpoint, all the quality of life impacts of that, which are beneficial in the case of patisiran. And then, for the cardiac outcomes, it show substantial decline in BNP, any changes in the structure of the heart in terms of reduced LV thickness, and also changes in functional outcome. And all of this was done specifically in a cardiac subgroup of patients. About half of the enrolled population in APOLLO had substantial involvement of the heart with cardiac amyloid from TTR, and in those patients we showed these outcomes. So we think the agency has a good understanding of the disease. We, obviously, gave a thorough background in our NDA documentation, and then we've addressed the different aspects of the disease

and the risk-benefit of the different aspects. And so we think that may be part of why they haven't requested an outcome, but really they'll have to address that. The other thing I think that has been very important in this outcome event is that, at least from our perspective and from the dialogue, I think there is a clear interpretation of data that we've provided in terms of risk-benefit. And so I think they -- I hope they'd be very encouraged by that. [They seem to be][sic].

153. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

154. These statements were also materially false and misleading when made because, despite Alnylam's assessment that hATTR Amyloidosis should be treated as a single disease with different manifestations, the requirements for obtaining an FDA label included a demonstration of the safety and efficacy for each desired indication of the drug, which was not done for cardiac manifestations of hATTR Amyloidosis in APOLLO III, and, as such, would require a completely separate study by Alnylam.

March 15, 2018, Barclays Global Healthcare Conference

155. On March 15, 2018, Defendant Greenstreet, on behalf of Alnylam, participated in the Barclays Global Healthcare Conference. During that conference, a Barclays analyst posed the following question to Defendant Greenstreet:

Okay. And then maybe we can switch gears talking about your patisiran in hereditary ATTR amyloidosis. So I know with the PDUFA day set now as August 11 this year, and we may have another drug also coming to the market, maybe I'll start with mechanistically, how do you see your approach with RNAi versus the other approaches (inaudible) and the differentiation there?"

156. In response, Defendant Greenstreet repeated the party line, again touting Patisiran's efficacy and safety profile:

Well, certainly, what we have in our hands with the dataset for patisiran I think is really quite remarkable. In terms of the efficacy that we've generated from the APOLLO study, which is the largest study ever done in patients with hATTR amyloidosis, where we saw highly significant improvement in the neurological endpoint, the mNIS+7 as well as a whole range of other secondary endpoints, quality of life, activity of daily living. Not just neurological endpoints and quality-of-life endpoints, *but also cardiac endpoints where we saw benefits in for instance (inaudible) BMP as well as echocardiographic improvements in left ventricular wall thickness and strain and also functional improvements in terms of the 10-meter walk test. So from an efficacy perspective, we believe we have really, really tremendous efficacy.* If you couple that with the safety profile that we've seen to date, where we've had very few adverse events, the only adverse events associated, really the drug infusion reactions, whereas, I think with the inotersen drug, I think you're seeing more discontinuation from the study actually whilst we had fewer discontinuation with patients receiving patisiran compared to placebo. They had something like 2 to 3x the number of discontinuations. So I think what's emerging as we look at these 2 medicines is a better efficacy profile as well as a better safety and tolerability profile. And we really feel that we have a best-in-class medicine here. So we're very keen to move to the regulatory process and be able to bring this patient -- this medicine to patients in the summertime.

157. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of

Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

158. These statements were also materially false and misleading when made because, despite Alnylam's assessment that hATTR Amyloidosis should be treated as a single disease with different manifestations, the requirements for obtaining an FDA label included a demonstration of the safety and efficacy for each desired indication of the drug, which was not done for cardiac manifestations of hATTR Amyloidosis in APOLLO III, and, as such, would require a completely separate study by Alnylam.

159. In a later exchange at the same conference, Gena Wang, a Barclays analyst, asked Defendant Greenstreet point blank: "[W]hat kind of a label would you expect to get [for Patisiran]?" Defendant Greenstreet, in response, represented that she expected a broad label and that included cardiac data on the label based on APOLLO III because, *inter alia*, hATTR Amyloidosis was "really one disease" with different manifestations:

I think given the positive data that we saw from APOLLO across all the endpoints that we tested, I talked about the neurological endpoints with mNIS, quality of life, the cardiac endpoints, et cetera. And given the fact that I think hATTR amyloidosis is now recognized as being, really, one disease; a multisystemic disease, but one disease with a mechanism of action of patisiran really knocking down TTR and

having such a profound effect on all the symptomatology. We believe that we will receive a broad label for the treatment of hATTR amyloidosis. Or we believe that all the endpoints that we studied in the APOLLO study, which showed both statistical and clinical meaningfulness, will be included in the label.

160. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

161. These statements were also materially false and misleading when made because, despite Alnylam's assessment that hATTR Amyloidosis should be treated as a single disease with different manifestations, the requirements for obtaining an FDA label included a demonstration of the safety and efficacy for each desired indication of the drug, which was not done for cardiac manifestations of hATTR Amyloidosis in APOLLO III, and, as such, would require a completely separate study by Alnylam.

May 3, 2018 10-Q

162. On May 4, 2018, Alnylam filed a Form 10-Q for the first fiscal quarter 2018 with the SEC (“2018 1Q 10-Q”) which was signed and certified by Defendants Maraganore and Soni.

In that 2018 1Q 10-Q Defendants stated in part:

In our patisiran APOLLO Phase 3 study in patients with polyneuropathy due to hATTR amyloidosis, the most commonly reported AEs that occurred more frequently in patisiran patients were peripheral edema and infusion-related reactions, or IRRs. These were generally mild to moderate in severity and only one patient discontinued from the APOLLO study due to an IRR. Compared to placebo, patisiran treatment was associated with fewer treatment discontinuations and fewer study withdrawals due to AEs. The incidence of SAEs across the patisiran and placebo groups was similar and the SAEs reported in two or more patients in the patisiran group included: diarrhea, cardiac failure, congestive cardiac failure, orthostatic hypotension, pneumonia and atrioventricular block complete. These were all considered unrelated to patisiran, except for one SAE of diarrhea. ***Deaths were recorded with a similar incidence across the patisiran and placebo treatment groups and no deaths were considered related to the study drug.***

163. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the

3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

164. In particular, while deaths may have been “recorded with a similar incidence across the patisiran (4.7 percent) and placebo (7.8 percent) treatment groups[,]” this statement was materially misleading because it omitted to disclose that cardiac deaths were recorded with a *significantly dissimilar incidence* for Patisiran and placebo.

165. The statements in the May 2018 10-Q appear verbatim in the November 7, 2017, and August 2, 2018 10-Qs.

May 3, 2018 Q1 2018 Earnings Call

166. On May 3, 2018, Alnylam hosted a conference call to discuss Alnylam’s first quarter 2018 earnings. On that earnings call, Defendant Vaishnaw again characterized Patisiran as efficacious and safe for cardiac patients based on APOLLO III:

In this regard, we were pleased to present new data just last week at the AAN conference from a post-hoc analysis of APOLLO data looking at the impact of patisiran treatment on hospitalization and mortality. In the figures on Slide 8, mortality and hospitalization events depicted over 18 months. The figure on the left depicts composite rate of all-cause hospitalization and mortality. As you can see, there's an approximately 50% decrease in this rate over 18 months in patisiran treated patients relative to placebo. Similarly, in the figure on the right, *we observed an approximately 45% reduction in the composite rate of cardiac hospitalization and all-cause mortality in patients treated -- in patisiran-treated patients relative to placebo. We believe these post-hoc data strengthen the existing body of evidence demonstrating that patisiran, if approved, has the potential to be a transformative treatment for patients with all forms of hereditary ATTR amyloidosis.*

As you may recall, with regards to safety and tolerability in the APOLLO study, there were 13 deaths overall, none of which were considered related to study drug, and *the frequency of deaths was lower in the patisiran group as compared to placebo.* Adverse events leading to treatment discontinuation were lower in the patisiran group as compared to placebo. The most commonly reported adverse events that occurred more frequently in patisiran-treated patients were peripheral

edema and infusion-related reactions. These were generally mild to moderate in severity.

We also recently presented additional data at the ISA meeting in March. ***It included results from the cardiac subpopulation, highlighting that patisiran treatment was associated with improvements in multiple measures of cardiomyopathy.*** These improvements, in conjunction with demonstrated benefits in neurologic improvement appears to be associated with favorable effects on gait speed, an important indicator of functional status. Furthermore, improvements across a range of echocardiographic parameters, including left ventricular wall thickness and left ventricular strain as well as a positive effect on levels of NT-proBNP, a cardiac stress biomarker, also ***speak to the potential for significant benefits of patisiran for patients with hATTR amyloidosis with cardiac involvement.***

167. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

168. These statements were also materially false and misleading when made because, despite Alnylam's assessment that hATTR Amyloidosis should be treated as a single disease with different manifestations, the requirements for obtaining an FDA label included a demonstration of the safety and efficacy for each desired indication of the drug, which was not done for cardiac

manifestations of hATTR Amyloidosis in APOLLO III, and, as such, would require a completely separate study by Alnylam.

169. On the same call, Terence C. Flynn, a Goldman Sachs analyst, asked Defendants Maraganore and Vaishnaw about the potential for a broad label for Patisiran:

Maybe just wondering if you guys are still confident you'll be able to secure a broad label for patisiran that would allow you to treat a range of hATTR patients?

170. Defendant Maraganore responded first, claiming that Alnylam was confident it would get a broad label based on the results of APOLLO III:

Thanks, Terence. Let me just touch on the first one and then Akshay should as well, and then we can go to the second question. Look, we believe that the totality of the APOLLO data for patisiran demonstrate an effective patisiran across the entirety of hATTR disease manifestations, *and the data are very strong across primary endpoints, secondary endpoints, exploratory endpoints and our submission to the FDA has been around a broad indication, and we believe the science and the data support that.* Now there's always a review process and so we will always have that discussion with the FDA, but we believe and still feel confident around our data set that supports a broad label. So Akshay, anything to add to that?

171. Defendant Vaishnaw followed up, echoing Defendant Maraganore's statements:

I mean, I agree with that. And I just think for sheer consistency of endpoints that with we -- the outcomes of the endpoints that we have both across neuropathy aspects, *cardiomyopathy aspects as well* as quality of life, activities of daily living, body mass and the autonomic features, including diarrhea, everything was in favor of the drug. And so that's obviously very encouraging and bodes for potential improvement in patients with a wide spectrum of disease.

172. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac

efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

173. These statements were also materially false and misleading when made because, despite Alnylam's assessment that hATTR Amyloidosis should be treated as a single disease with different manifestations, the requirements for obtaining an FDA label included a demonstration of the safety and efficacy for each desired indication of the drug, which was not done for cardiac manifestations of hATTR Amyloidosis in APOLLO III, and, as such, would require a completely separate study by Alnylam.

174. Eric William Joseph, a JP Morgan analyst, also asked Defendant Maraganore about the anticipated label for Patisiran:

It's Eric in for Anupam. I just wanted to follow up on your comments about the potential breadth of hereditary ATTR label with patisiran. And just wondering whether they similarly apply to CHMP as well as FDA, are there sort of any differences in the conversations that you're having around label breadth between the different agencies? And secondly, it sounds like from their recent earnings call that Pfizer is also looking to reengage or repursue tafamidis in the U.S. for polyneuropathy. I'm just wondering, based on what you're hearing from physicians, whether you anticipate tafamidis either through off-label use or clinical development being sort of a hurdle to commercial uptake and in predominantly polyneuropathy patients, do you kind of see a window with which you kind of have to kind of execute on to establish patisiran as a standard of care in the population?

175. Once again, Defendant Maraganore stood confidently by a broad label for Patisiran based on APOLLO II, and touted Patisiran in comparison with rival Pfizer's Tafamidis, which was designed to treat cardiomyopathy manifestations of hATTR Amyloidosis:

Yes. Let me tackle the questions, and then Akshay and Barry could jump in, Yvonne as well. The first question on EMA. Well, firstly, we're not, Eric, going to go into details about our discussions, which are confidential with regulators and we're dealing with a competitive landscape as well, so we're going to be protective around that. ***But we have -- we do believe the data from patisiran and APOLLO support the broad label***, and we believe that, that broad label supported both in the U.S. and in Europe. So we've kept consistent with that. And -- but these are discussions that are still ongoing with regulators, and ultimately we'll see where the labels end up. ***But we do believe the data support the breadth of impact across the entirety of hereditary ATTR***. So that's the answer to your question there.

Regarding your second question. Yes, on tafamidis, we think it's possible that they will -- I mean, if I were them, I would look for a broad label as well, including the neuropathy segment, that is possible that they get that with the FDA. As you know, they were rejected in the U.S. because they didn't hit their primary endpoint, but they were approved in Europe. So I think it's very possible that they get a polyneuropathy on their label. But I think that we know what tafamidis does in that setting and it slows down disease a little bit, and if you go to the 80-milligram dose, you're not going to do better than diflunisal, which is a much better stabilizer than tafamidis, and we know what diflunisal does in that setting. It slows things down a little bit, but people still progress. So I don't think there's any doubt in the minds of physicians who treat these patients that the stabilizers have really shown a relatively incremental impact on neuropathy progression in these patients. So they may well get the label. That's great. Terrific. But I don't think it will change how physicians look at using an agent like patisiran, which really has a very strong impact compared to an agent like tafamidis or for that matter diflunisal, which really only slows down progression.

176. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from

the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

177. These statements were also materially false and misleading when made because, despite Alnylam's assessment that hATTR Amyloidosis should be treated as a single disease with different manifestations, the requirements for obtaining an FDA label included a demonstration of the safety and efficacy for each desired indication of the drug, which was not done for cardiac manifestations of hATTR Amyloidosis in APOLLO III, and, as such, would require a completely separate study by Alnylam.

May 8, 2018, Deutsche Bank Healthcare Conference

178. On May 8, 2018, Defendant Greenstreet, on behalf of the Company, participated in the Deutsche Bank Healthcare Conference. At that conference, Defendant Greenstreet emphasized Patisiran's safety for cardiac patients – six months after the Defendants finished reviewing APOLLO III data in (at the latest) November 2017 and learned that there was a 3.5:1 cardiac death ratio for Patisiran to placebo, substantially the same as the 4:1 ratio that ended the Revusiran trial:

I'd like to spend a few moments on the results that we got with patisiran and key exploratory endpoints for cardiac subpopulation. We showed benefits in a very important biomarker for assessing cardiac stress, the NT-proBNP. And you can see here improvements with -- compared to placebo as well as important echocardiographic features, left ventricular wall thickness and longitudinal strain. And importantly all of these features wrapped into improving the patient's functional status, as you can see here in terms of benefits in gait speed with patisiran compared to the deterioration that you see in a 10-minute walk test with placebo.

So very important that not only have we impacted on key neurological endpoints and quality of life endpoints, but also really addressing the needs of patients with cardiomyopathy. ***You can see here a post-hoc analysis that we presented recently showing hospitalization and death events with patisiran compared to placebo.*** This was a post-hoc analysis. On the left-hand side, you can see a chart, which shows the composite rate of all-course hospitalization and mortality with patisiran compared to placebo. And we were able to demonstrate an approximately 50% reduction in event rate in the placebo arm. Again, on the right-hand side chart, where you look -- where we looked at composite rates of cardiac hospitalization, all-cause mortality, patisiran was able to achieve an approximately 45% reduction in event rate. So I think very important data demonstrating the utility of patisiran in patients with respect to cardiac hospitalization, all-cause hospitalization and mortality. ***When we turn to safety and tolerability, there were 13 deaths in the APOLLO study and no deaths were considered related to study drug. There's actually a lower percentage of deaths in patisiran versus placebo. There were also lower adverse events with discontinuations in patients that received patisiran compared to placebo, and I think it's a very important finding when you consider safety and tolerability with a investigational medicine.***

The most common adverse event more frequently observed in the patisiran arm versus placebo included peripheral edema and infusion-related reaction. But both of these adverse events decreased over time and the IRRs led to discontinuation in only one patient; peripheral edema leading to discontinuations in no patients.

Also notably, there was encouraging safety and tolerability in the cardiac subpopulation. No safety signals related to steroid premedication; no safety signals regarding liver function tests, hematology, including thrombocytopenia or renal dysfunction related to patisiran. So I think a really encouraging emerging safety and tolerability profile for patisiran.

179. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety

concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

180. These statements were also materially false and misleading when made because, despite Alnylam's assessment that hATTR Amyloidosis should be treated as a single disease with different manifestations, the requirements for obtaining an FDA label included a demonstration of the safety and efficacy for each desired indication of the drug, which was not done for cardiac manifestations of hATTR Amyloidosis in APOLLO III, and, as such, would require a completely separate study by Alnylam.

June 6, 2018, Jefferies Global Healthcare Conference

181. On June 6, 2018, at the Jefferies Global Healthcare Conference, Maurice Thomas Raycroft, a Jefferies LLC analyst asked, in relevant part, as follows: "Maybe if you can talk about what you think is going to end up in the label? And what are some different scenarios and how that could play out?" In response, Defendant Greenstreet was still very confident of FDA approval of a broad label:

Yes. I mean, that's a really good question. And I think you're obviously right. We feel that we have been able to deliver some pretty impressive data with respect to cardiac endpoints. We actually had some prespecified cardiac endpoints to study, and I think that's an important point to make. ***We also did a post-hoc analysis, where we looked at hospitalizations and mortality, and actually showed a 45% improvement in hospitalization and mortality compared to placebo.*** I think this is, again, another important data point even though not being prespecified that may not find its way into label. With respect to exactly what we'll get in the label, we're very close now. So we all know, and we no longer have to speculate. ***We feel we have great cardiac data. We feel that hATTR amyloidosis is one disease, and we've been able to demonstrate that we can really address the key pathophysiology of disease and knock down TTR and impact on all the symptomatology that you see with hATTR. So we think we have a really good compelling proposition here.*** At the end of the day, we're going to have to leave it to the FDA to decide how they want to think about that.

182. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

183. These statements were also materially false and misleading when made because, despite Alnylam's assessment that hATTR Amyloidosis should be treated as a single disease with different manifestations, the requirements for obtaining an FDA label included a demonstration of the safety and efficacy for each desired indication of the drug, which was not done for cardiac manifestations of hATTR Amyloidosis in APOLLO III, and, as such, would require a completely separate study by Alnylam.

June 14, 2018 Goldman Sachs Global Healthcare Conference

184. On June 14, 2018 Alnylam presented at the Goldman Sachs Global Healthcare Conference. At that conference, Defendant Soni described Patisiran's strong efficacy for cardiac patients:

So as you know, this disease is pretty ultra orphan disease *and as we have shown efficacy in all of the specs off, cardiomyopathy* and polyneuropathy and into -- whether it's neurologic manifestations. So we believe it's unfair to give a range, but it should be priced pretty much as other orphan drugs are priced, which should be in 6 digits. I think that's what we could say right now. We're not giving any specific guidance right now.

185. These statements were materially false and misleading when made because they fundamentally misrepresented the efficacy and safety of APOLLO III for cardiac patients and omitted material facts; namely, that (i) APOLLO III was not designed to test the efficacy of Patisiran for cardiomyopathy and cardiac manifestations of hATTR Amyloidosis; (ii) APOLLO III provided no cardiac efficacy data to the FDA; (iii) obtaining FDA approval without any cardiac efficacy data for a broad-based label that would include cardiomyopathy or even cardiac data from the APOLLO III trial was impossible, and a completely new study would have to be designed and conducted to support the efficacy of Patisiran for cardiac patients; and (iv) there were 7 cardiac-related deaths on Patisiran and only 1 on the placebo, for a 3.5:1 ratio, which posed a serious safety concern militating strongly against FDA approval of a dual label or cardiac data on the label (the 3.5:1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial).

186. These statements were also materially false and misleading when made because, despite Alnylam's assessment that hATTR Amyloidosis should be treated as a single disease with different manifestations, the requirements for obtaining an FDA label included a demonstration of the safety and efficacy for each desired indication of the drug, which was not done for cardiac manifestations of hATTR Amyloidosis in APOLLO III, and, as such, would require a completely separate study by Alnylam.

The Market Begins to Learn What Defendants Knew Was Inevitable – The FDA Would Not Approve Patisiran For Cardiomyopathy and Would Not Allow Cardiac Data on the Label

187. On August 10, 2018, Alnylam announced that Patisiran received FDA approval for polyneuropathy only. Not only did the FDA decline to approve Patisiran for a broader-based label that included cardiomyopathy, or mixed polyneuropathy and cardiomyopathy manifestations, but the FDA did not allow any cardiac data from APOLLO III to appear on the newly-approved drug's label.

188. On August 10, 2018, the FDA also put out a press release announcing the news. That release provided, in pertinent part:

FDA approves first-of-its kind targeted RNA-based therapy to treat a rare disease

For Immediate Release:

August 10, 2018

The U.S. Food and Drug Administration today approved Onpattro (patisiran) infusion for the treatment of peripheral nerve disease (polyneuropathy) caused by hereditary transthyretin-mediated amyloidosis (hATTR) in adult patients. This is the first FDA-approved treatment for patients with polyneuropathy caused by hATTR, a rare, debilitating and often fatal genetic disease characterized by the buildup of abnormal amyloid protein in peripheral nerves, the heart and other organs. It is also the first FDA approval of a new class of drugs called small interfering ribonucleic acid (siRNA) treatment....

189. Notably, the FDA's press release did not disclose to the market why the agency declined to allow a broader label for Patisiran or why it declined to allow Alnylam to include any cardiac data on Patisiran's label. Nor did the FDA address the likelihood or potential timeline for Alnylam to obtain such a broad label for Patisiran, leaving investors to draw their own conclusions as to Patisiran's future potential.

190. During an August 10, 2018 conference call to discuss the limited FDA approval, Defendant Maraganore attempted to mitigate the harm caused by the FDA's limited approval for

Patisiran, in relevant part, by stating that “[w]hile the indication of the U.S. label is for patients with polyneuropathy and the label does not include cardiac data, we do look forward to working with the FDA to expand the [Patisiran] label more broadly in the future.” In other words, Defendant Maraganore gave the market false hope that Alnylam at least had the basis based on APOLLO III and continued confidence to believe that a broader label for Patisiran would be forthcoming.

191. This statement was materially false and misleading when made because (i) the FDA declined to approve Patisiran for cardiomyopathy treatment, or even allow cardiac data on a Patisiran label, because APOLLO III lacked a primary cardiomyopathy endpoint and failed to test the efficacy or safety of the drug for that purpose; and (ii) the 3.5 to 1 drug to placebo cardiac death ratio posed a serious safety concern for the (the 3.5 to 1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial). This statement was also materially false and misleading when made because Defendant Maraganore knew or was reckless in not knowing that, despite Alnylam’s assessment that hATTR Amyloidosis should be treated as a single disease with different manifestations, the requirements for obtaining an FDA label included a demonstration of the safety and efficacy for each desired indication of the drug, which was not done for cardiac manifestations of hATTR Amyloidosis in APOLLO III, and, as such, would require a completely separate study by Alnylam.

192. Because of the critical importance of Alnylam’s failure to achieve a broad label for Patisiran, as Defendants confidently claimed they would, analysts on the August 10, 2018 call were all over the issue – as they had been for almost a year. For example, a Barclays analyst sought clarity into whether, in light of the failure to achieve a broad Patisiran label or cardiac data on the label at this time, the label could possibly be expanded in the future:

Gena Wang [Barclays Bank PLC]...So my question is, I think, John, you also mentioned that you have a plan to expand the label. Just wondering, what will be the timeline you are thinking about and what additional data you'll be adding? And then what kind of label expansion you were talking about? Is that expanded to the pure cardiomyopathy patient population in the hereditary ATTR subcategory?

193. In response, Defendant Maraganore had no details to provide other than that he was confident in the results of APOLLO III as it related to cardiac patients and the possibility of expanding the label for Patisiran would be an ongoing discussion with the FDA:

Defendant Maraganore [Alnylam]: Thanks, Gena, for the question. So -- and maybe Pushkal wants to comment as well. I mean first of all, we had very collaborative discussions with FDA.... And during the course of those discussions, the agency did feel that we should come back and speak with them about how we expand the label in the most efficient manner possible.

194. This statement was materially false and misleading when made because Defendant Maraganore knew or was reckless in not knowing that (i) the FDA declined to approve Patisiran for cardiomyopathy treatment, or even allow cardiac data on a Patisiran label, because APOLLO III lacked a primary cardiomyopathy endpoint and failed to test the efficacy or safety of the drug for that purpose; and (ii) the 3.5 to 1 drug to placebo cardiac death ratio posed a serious safety concern for the (the 3.5 to 1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial). This statement was also materially false and misleading when made because Defendant Maraganore knew or was reckless in not knowing that, despite Alnylam's assessment that hATTR Amyloidosis should be treated as a single disease with different manifestations, the requirements for obtaining an FDA label included a demonstration of the safety and efficacy for each desired indication of the drug, which was not done for cardiac manifestations of hATTR Amyloidosis in APOLLO III, and, as such, would require a completely separate study by Alnylam.

195. In fact, Defendants knew all along that APOLLO III's failure to test the cardiac efficacy of Patisiran doomed a cardiomyopathy label for Patisiran as well as the inclusion of cardiac data on the label. Nevertheless, after the failure of Revusiran, Defendants still doubled down and sold the market on the drug's potential for a broad label that would recapture the lost cardiac patient market when Revusiran failed.

196. Another colloquy on the call also concerned the failure to achieve a broad label that included cardiomyopathy:

Unidentified Analyst: Great. A quick follow up, if I may. I was wondering if -- does this change your thinking about how you target the cardiologist population both in the U.S. and/or EU based on the label as it is right now?

Defendant Maraganore [Alnylam]: Yes. Barry, do you want to handle that?

Barry E. Greene [Alnylam]: Yes, it's a great question. So as we talked about earlier, this is a multisystem disease where multiple specialists see these patients. So we will be targeting cardiologists, neurologists, gastroenterologists and other physician groups that touch these patients. Because what we're looking for is polyneuropathy in this disease, and that polyneuropathy can in fact be found by multiple disciplines.

197. This statement was materially false and misleading when made because (i) the FDA declined to approve Patisiran for cardiomyopathy treatment, or even allow cardiac data on a Patisiran label, because APOLLO III lacked a primary cardiomyopathy endpoint and failed to test the efficacy or safety of the drug for that purpose; and (ii) the 3.5 to 1 drug to placebo cardiac death ratio posed a serious safety concern for the (the 3.5 to 1 drug to placebo death ratio was basically the same as the 4:1 ratio that ended the ENDEAVOUR trial). This statement was also materially false and misleading when made because these defendants knew or were reckless in not knowing that, despite Alnylam's assessment that hATTR Amyloidosis should be treated as a single disease with different manifestations, the requirements for obtaining an FDA label included a demonstration of the safety and efficacy for each desired indication of the drug, which was not

done for cardiac manifestations of hATTR Amyloidosis in APOLLO III, and, as such, would require a completely separate study by Alnylam.

198. After the August 10, 2018 conference call, Alnylam's stock price fell from \$97.38 per share on August 10, 2018, to close at \$90.95 per share on the next trading day, August 13, 2018, a decline of \$6.43 per share or approximately 6%. Alnylam lost approximately \$600 million in market capitalization.

199. Based on the bullish representations made by Defendants throughout the Class Period concerning Patisiran's potential to secure a broad-based label, or, at a minimum, obtain a label that would include cardiac data from APOLLO III, securities analysts were surprised by the outcome of the FDA's labeling determination. For example, on August 12, 2018, Do Kim, a BMO Capital securities analyst writing in response to the FDA's labelling decision stated, in relevant part, that: "*We believe the consensus expected cardiac data on the U.S. label at minimum, following management comments suggesting the Onpattro SmPC would include cardiac results.*"

200. Similarly, on the same date, Ritu Baral, a Cowen securities analyst, reported that "ALNY had requested a broad label for TTR amyloidosis without phenotypic restriction. *Our expectation was that FDA would issue a narrow label for FAP but allow inclusion of the cardiac benefit data* in the Clinical Studies section of the label, in line with the recent CHMP recommendation. *The actual label released today however makes no reference to any cardiac-related outcomes measured in APOLLO.*"

201. On August 13, 2018, Goldman Sachs securities analyst Terence Flynn also noted that the "lack of cardio data in the U.S. label was disappointing and could represent a disadvantage vs Pfizer's competitor drug tafamadis."

202. On August 13, 2018, David N. Lebowitz and Matthew Harrison, Morgan Stanley securities analysts, wrote that: “[a]lthough the approval of ONPATTRO gives Alnylam its first commercially available drug, the indication granted by the FDA is highly restrictive versus the broad label that was sought by company mgt. that would have covered all hATTR patients.” Accordingly, Morgan Stanley lowered its price target for Alnylam from \$99.00 to \$93.00.

203. In another August 13, 2018 analyst report, Christopher Marai, a Nomura/Instinet analyst, cut his price target on Alnylam from \$86 to \$73, noting that competition from Pfizer’s tafamadis, Prothena’s PRX0004 and others would “decimat[e] the market opportunity for [Patisiran] in 18 months-plus time. In other words, the failure of Revusiran to achieve a label that included cardiac data would clear the path for Alnylam’s competitors to gain market advantage vis a vis the cardiac patient population.

204. Then, on August 27, 2018, Pfizer announced positive Tafimidis results for hATTR cardiomyopathy:

Pfizer Inc. (NYSE:PFE) announced today the primary results from the Tafamidis Phase 3 Transthyretin Cardiomyopathy (ATTR-ACT) study, which showed tafamidis significantly reduced the hierarchical combination of both all-cause mortality and frequency of cardiovascular-related hospitalizations compared to placebo over a 30-month period (P=0.0006) in patients with wild-type or variant (hereditary) transthyretin amyloid cardiomyopathy (ATTR-CM).

205. On the same day, Morgan Stanley made it clear that Alnylam was still a long way off from an hATTR cardiomyopathy drug – and that the Company’s best shot going forward was not Patisiran but ALN-TTR. In a report entitled “Tafimidis Benefit is Intriguing, But Alnylam Still 2+ Years From market for Cardio TTR”, analyst David Lebowitz stated that “considering the FDA’s recent approval for Onpattro [Patisiran] is for polyneuropathy patients, questions around the strength of tafimidis is [sic] not crucial as ALNY has 2+ years of work on ALN-TTRscO2 before they can reach market for ATTR-CM patients.”

The Market Learns the Full Extent of the APOLLO III Failure – Alnylam Provided No Cardiac Efficacy Data to the FDA and Tried to Change Cardiac Death Data After its NDA Submission

206. On September 12, 2018, multiple analysts published reports analyzing a voluminous 485-page FDA report had that just been released concerning Alnylam’s FDA submission for Patisiran. For example, on September 12, 2018, Christopher Marai, a Nomura analyst, wrote:

The FDA’s Center for Drug Evaluation and Research (CDER) just released ALNY’s ONPATTRO NDA review document (report here). The 485-page document contains FDA analyses of the NDA submission, including: imbalances in mortality, the nature of cardiac events that occurred in the APOLLO trial, *and the lack of efficacy data in cardiac patients.... We believe some comments on the lack of cardiac efficacy call into question claims made by Alnylam in this regard.*

Among other things, Marai noted that the FDA Report “highlights greater risk” with respect to cardiac patients based on the data of APOLLO III.

207. The FDA Report, which was dated August 10, 2018 but not released publicly until on or around September 12, 2018, detailed the scope of the FDA’s denial of Alnylam’s bid for a broad label and the inclusion of cardiac data on the label for Patisiran based on the data of APOLLO III.

208. First, the FDA Report contained incredibly damning facts about Patisiran’s inability to show “any efficacy data” for cardiomyopathy treatment – informing the market that Alnylam was really back to square one with Patisiran as it related to the cardiac patient population:

Study ALN-TTR02-004 [(i.e., Apollo)] does not provide any cardiac efficacy data. Imaging and serum biomarkers such as global longitudinal strain and NTproBNP do not measure how a patient feels, functions, or survives, nor are they known to predict how a patient feels, functions, or survives and hence do not measure a clinical benefit...

Based on the mechanism of action of Patisiran, it is theoretically possible that it might be beneficial for the non-polyneuropathy symptoms in patients with hATTR. However, any such benefits have not been established in the current development program. Although

the applicant included a cardiac subpopulation in the placebo-controlled Study 004 and measured some cardiac biomarkers, as discussed in Section 6.1, *the FDA cardiology consultant concluded that ‘Study ALN-TTR02-004 does not provide any cardiac efficacy data’.*

209. As alleged above, Defendants knew or recklessly disregarded that it was impossible for APOLLO III to serve as the basis for FDA approval of a cardiac indication for Patisiran because the clinical trial did not test for, and therefore did not yield, efficacy data for the treatment of cardiac patients.

210. Defendant Maraganore had represented to analyst Gena Wang on the August 10, 2018 conference call that future expansion of the label was quite possible – claiming that “the agency did feel that we should come back and speak with them about how we expand the label in the most efficient manner possible.” In reality, however, with the FDA stating that Alnylam “does not provide any cardiac efficacy data”, the Company had little if anything to build on – particularly because time was of the essence as Alnylam was racing against Pfizer to bring the first hATTR cardiomyopathy drug to market. Instead, Alnylam would be forced to go back to the drawing board to design an entirely new study that could support the safety and efficacy of Patisiran in treating patients with cardiomyopathy manifestations of hATTR Amyloidosis.

211. Notably, the FDA Report also spoke at length about Patisiran’s safety in cardiac patients and specifically Alnylam’s attempt to re-characterize two of the cardiac placebo deaths, in relevant part, as follows:

In the placebo-controlled Study 004 [APOLLO III], 7 deaths in the patisiran group (4.7%) were possibly related to heart failure (cause characterized as sudden cardiac death or heart failure), whereas there was only one such death in the placebo group (with 2:1 randomization)...

Originally, all 7 deaths in the patisiran group (4.7%) were considered to be cardiovascular in nature, with only 1 cardiovascular death in placebo-treated patients (1.3%). The applicant subsequently convened an independent and blinded adjudication committee to review the cases of death from Study 004 and classify

them as cardiovascular or non-cardiovascular.... With adjudication, all 7 deaths in the patisiran group remained attributed to cardiovascular causes, whereas the causes of death for 2 patients in the placebo group were reclassified from non-cardiovascular to cardiovascular ...(increasing the total number of cardiovascular deaths to 3 in the placebo group (3.9%)).... Importantly, however, both of the cardiovascular deaths added to the placebo group were attributed to stroke, not heart failure.... Thus, with respect to deaths plausibly related to heart failure, the 7 to 1 difference (4.7% in the patisiran group vs. 1.3% in the placebo group) remains, and this difference is concerning.

212. Thus, in light of the lack of efficacy data for cardiac patients and serious safety concerns witnesses for those patients in APOLLO III, the FDA flatly “recommend[ed] that, if approved, the indication in the label should explicitly state that Onpattro is intended solely for treatment of Familial Amyloid Polyneuropathy[.]” Moreover, despite the bullishness that Defendants projected to the market about the future likelihood of securing a broader-based label for Patisiran, the FDA’s report made clear that Alnylam was nowhere near gaining such approval, as it had not yet provided any support demonstrating the efficacy of Patisiran, and the limited data from APOLLO III raised “serious” cardiac safety concerns about the drug. In other words, Alnylam competitors Pfizer and Ionis would gain years of market advantage if their drugs were approved first. And this is precisely what happened, in May 2019, the FDA granted Pfizer’s request to approve Tafimidis for hATTR cardiomyopathy.

213. After the adverse September 12, 2018 news was revealed, Alnylam’s stock price fell an additional \$5.60, or over 5.5%, to close at \$94.75 per share on September 12, 2018. In total, accounting for the two disclosures, the fraud perpetrated by Defendants had the effect of erasing approximately \$1.2 billion in market capitalization for Alnylam.

ALLEGATIONS OF SCIENTER

214. As alleged herein, each of the Individual Defendants acted with scienter in that they knew, or recklessly disregarded, that the public documents and statements they issued and

disseminated to the investing public in the name of Alnylam or in their own name during the Class Period were materially false and misleading.

215. The Individual Defendants knowingly and substantially participated or acquiesced in the issuance or dissemination of such statements and documents as primary violations of the federal securities laws.

216. The Individual Defendants, by virtue of their receipt of the APOLLO III data, their control over, and/or receipt and/or modification of Alnylam's allegedly materially misleading misstatements, were active and culpable participants in the fraudulent scheme alleged herein.

217. As highly educated PhDs and pharmaceutical executives, the Individual Defendants were intimately acquainted with clinical trials and the FDA regulations surrounding them. In particular, they were well aware that it is extremely rare for the FDA to approve a drug when there is no primary endpoint linked to the disease indicated.

218. The Individual Defendants knew and/or recklessly disregarded the falsity and misleading nature of the information that they caused to be disseminated to the investing public. The fraudulent scheme described herein could not have been perpetrated during the Class Period without the knowledge and complicity or, at least, the reckless disregard of the personnel at the highest levels of the Company, including the Defendants.

219. The Individual Defendants, because of their positions with Alnylam, made and/or controlled the contents of the Company's public statements during the Class Period. Each Individual Defendant was provided with or had access to the information alleged herein to be false and/or misleading prior to or shortly after their issuance and had the ability and opportunity to prevent their issuance or cause them to be corrected. Because of their positions and access to material non-public information, these Individual Defendants knew or recklessly disregarded that

the adverse facts specified herein had not been disclosed to and were being concealed from the public and that the positive representations that were being made were materially false and misleading. As a result, each of these Individual Defendants is responsible for the accuracy of Alnylam's corporate statements and is therefore responsible and liable for the representations contained therein.

1. The Individual Defendants' Insiders Sales of Over \$66 Million of Alnylam Stock At Suspicious Times Strongly Supports an Inference of Scienter

220. The Individual Defendants were highly motivated to commit the fraud alleged herein in order to reap tens of millions of dollars in insider sales proceeds before the market learned the truth about APOLLO III. They were also motivated to make the materially false and misleading statements and omissions alleged *supra* because doing so artificially increased Alnylam's stock price and, thus, increased their proceeds from their insider sales.

221. For the reasons detailed *supra*, the Individual Defendants knew or were reckless in not knowing that the FDA would not grant Patisiran a broad-based label or one that would include cardiac data on the Patisiran label from APOLLO III. The Individual Defendants knew or recklessly disregarded this throughout the Class Period because of the fundamentally flawed way in which they structured APOLLO III as it related to cardiomyopathy and/or cardiac manifestation of hATTR Amyloidosis. The Individual Defendants' knowledge of this predated the start of the Class Period and certainly would have been further appreciated by no later than September 20, 2017 when Alnylam announced the top line results for APOLLO III. Their knowledge of these issues was further solidified when they announced that they finished reviewing the APOLLO III data on November 2, 2017.

222. While Alnylam's stock price was artificially inflated due to the Individual Defendants' false and misleading statements, Alnylam insiders sold a whopping \$66.1 million of Alnylam stock while in possession of material, adverse information:

<u>Insider</u>	<u>Date</u>	<u>Shares Sold</u>	<u>Price</u>	<u>Proceeds</u>
Barry Greene (President)	09/20/2017	76,815	\$100.00	\$7,681,500.00
	10/02/2017	85,316	\$125.00	\$10,664,500.00
	03/14/2018	2,884	\$140.43	\$405,000.00
	03/14/2018	7,250	\$141.74	\$1,027,620.00
	03/14/2018	9,217	\$142.68	\$1,315,080.00
	03/14/2018	8,644	\$143.58	\$1,241,110.00
	03/14/2018	9,165	\$144.67	\$1,325,900.00
	03/14/2018	1,300	\$145.41	\$189,033.00
Total Greene		200,591		\$23,849,743
Yvonne Greenstreet (EVP, COO)	3/26/2018	100	\$141.47	\$14,147.00
	3/26/2018	419	\$137.78	\$57,729.80
	3/26/2018	2,394	\$137.09	\$328,193.00
	3/26/2018	4,308	\$136.00	\$585,888.00
	8/30/2018	2,500	\$120.00	\$300,000.00
Total Greenstreet		9,721		\$1,285,957.80
John Maraganore (CEO)	11/15/2017	600	\$130.22	\$78,130.80
	11/15/2017	4,850	\$129.57	\$628,414.00
	11/15/2017	10,571	\$128.48	\$1,358,200.00
	11/15/2017	7,120	\$127.54	\$908,085.00
	11/15/2017	28,399	\$126.60	\$3,595,400.00
	11/15/2017	22,460	\$125.54	\$2,819,720.00
	11/22/2017	2,683	\$132.73	\$356,115.00
	11/22/2017	20,433	\$131.82	\$2,693,480.00
	11/22/2017	25,036	\$130.88	\$3,276,710.00
	11/22/2017	25,263	\$129.97	\$3,283,430.00
	7/25/2018	1,400	\$106.25	\$148,750.00
	7/25/2018	34,995	\$105.83	\$3,703,520.00
	7/25/2018	7,758	\$104.83	\$813,271.00
	7/25/2018	3,847	\$103.69	\$398,895.00
	7/25/2018	2,000	\$102.51	\$205,020.00

Total Maraganore		197,415		\$24,267,140.80
Akshay Vaishnaw (EVP/Pres R&D)				
	10/30/2017	3,693	\$122.79	\$453,463.00
	10/30/2017	17,755	\$121.69	\$2,160,610.00
	10/30/2017	11,418	\$120.78	\$1,379,070.00
	10/30/2017	800	\$119.79	\$95,832.00
	3/14/2018	6,380	\$145.27	\$926,823.00
	3/14/2018	20,172	\$144.53	\$2,915,460.00
	3/14/2018	19,213	\$143.46	\$2,756,300.00
	3/14/2018	21,336	\$142.57	\$3,041,870.00
	3/14/2018	15,000	\$141.69	\$2,125,350.00
	3/14/2018	6,453	\$140.45	\$906,324.00
Total Sales -- Vaishnaw		122,220		\$16,761,102.00
TOTALS		529,947		\$66,163,943.60

223. Defendants' insider sales were suspicious in timing and amount.

A. Defendant Greene

224. For example, after selling only \$1.3 million of Alnylam stock in 2016, and \$8.4 million in 2015, Defendant Greene **sold over \$18 million in Alnylam stock in only 12 days in Septemner/October 2017.** Defendant Greene made his sales on September 22, 2017 – after the Company announced that it received the top-line APOLLO III data – and on October 2, 2017, just 12 days later.

225. Defendant Greene also sold Alnylam shares in suspicious amounts. Defendant Greene's September 22, 2017 sale of 76,815 shares comprised almost half – 46% – of his Alnylam

shares. Likewise, Defendant Greene's October 2, 2017 sale of 85,316 shares also comprised almost half – 46% – of his Alnylam shares.¹⁰

226. Defendant Greene's sales were made pursuant to 10b5-1 trading plans, but he entered into those plans while in possession of material adverse information about Patisiran that was not disclosed to the market. Specifically, Defendant Greene's September and October 2017 sales were made pursuant to a Rule 10b5-1 trading plan that he adopted on January 23, 2017—when he was already aware of the flawed design of APOLLO III for testing the safety and efficacy of Patisiran for cardiac manifestations of hATTR Amyloidosis. Defendant Greene's March 2018 sales likewise were made pursuant to a Rule 10b5-1 trading plan that he adopted on January 11, 2018 – when he was already aware of both the flaws in the study and the serious adverse cardiac death rates from the APOLLO III data. Accordingly, Defendant Greene's insider sales are highly probative of scienter.

B. Defendant Maraganore

227. As with Defendant Greene, Defendant Maraganore sold huge amounts of his Alnylam stock at suspicious times and in suspicious amounts. Specifically, Defendant Maraganore sold a total of approximately \$19 million of Alnylam stock on November 15, 2017 and November 22, 2017 – just weeks after Alnylam announced that it had finished reviewing the APOLLO III data that showed a serious safety issue (the drug to placebo cardiac death ratio of 3.5 to 1). Notably, just before these sales were made, Defendant Maraganore had trumpeted Patisiran's cardiac efficacy and safety on November 2, 2017. *See* ¶93.

¹⁰ Greene exercised rights to purchase approximately 85,316 shares on October 2, 2017 and then immediately sold those shares.

228. Defendant Maraganore also sold \$5.2 million worth of Alnylam stock on July 25, 2018 – one month before the FDA revealed that (i) it would approve Patisiran’s label for neuropathy, but not for cardiomyopathy; and (ii) it would not allow any cardiac data from APOLLO III on the Patisiran label.

229. The amounts of Defendant Maraganore’s stock sales are also highly suspicious. During the Class Period, Defendant Maraganore sold **\$24.2 million** worth of Alnylam stock within 8 months (between November 2017 and July 2018). In contrast, Maraganore sold only \$6 million of Alnylam stock during 2016 and \$12 million during 2015.

230. Defendant Maraganore’s sales likewise were made pursuant to 10b5-1 trading plans, but he too entered into those plans while in possession of material adverse information about Patisiran that was not disclosed to the market. Specifically, Defendant Maraganore’s 2017 sales were made pursuant to a Rule 10b5-1 trading plan that he adopted on January 13, 2017 – when he was already well aware of the fundamental flaws in APOLLO III for testing the safety and efficacy of Patisiran for cardiac manifestations of hATTR Amyloidosis. Moreover, Defendant Maraganore’s 2018 sales were made pursuant to a Rule 10b5-1 trading plan that he adopted on January 16, 2018 – when he was already aware of both the flaws in APOLLO III and the serious adverse cardiac death rates from the APOLLO III data. Accordingly, Defendant Maraganore’s insider sales are highly probative of scienter.

C. Defendant Vaishnaw

231. As with Greene and Maraganore, Defendant Vaishnaw also sold substantial amounts of his Alnylam shares at suspicious times and in suspicious quantities. Specifically, Defendant Vaishnaw sold \$4 million of his Alnylam stock on October 30, 2017 – just two days before Alnylam announced that it had finished reviewing the APOLLO III data. Notably,

Defendant Vaishnaw made glowing statements about Patisiran on September 20, 2017, November 2, 2017, and November 7, 2017 -- before and right after his insider sales.

232. Defendant Vaishnaw's stock sales were also suspicious in amount. During the Class Period, Defendant Vaishnaw sold **\$16.7 million** worth of his Alnylam stock. In contrast, Vaishnaw sold only \$3 million of his Alnylam stock in 2013, \$4.8 million in 2014, \$2.1 million in 2015, and \$1.3 million in 2016.

233. Defendant Vaishnaw's sales were likewise made pursuant to 10b5-1 trading plans, but he too entered into those plans while in possession of material adverse information about Patisiran that was not disclosed to the market. Specifically, Defendant Vaishnaw's October 2017 sales were made pursuant to a Rule 10b5-1 trading plan that he adopted on August 29, 2017 – when he was already well aware of the fundamental flaws in APOLLO III for testing the safety and efficacy of Patisiran for cardiac manifestations of hATTR Amyloidosis. Moreover, Defendant Vaishnaw's March 2018 sales were made pursuant to a Rule 10b5-1 trading plan that he adopted on January 10, 2018 – when he was already aware of both the flaws in APOLLO III and the serious adverse cardiac death rates from the APOLLO III data. Accordingly, Defendant Vaishnaw's insider sales are highly probative of scienter.

D. Defendant Greenstreet

234. Defendant Greenstreet's insider sales were also highly suspicious. Before selling **\$1.3 million** worth of her Alnylam stock in 2018, Defendant Greenstreet had made no prior stock sales since she started with the Company in September 2016.

235. Defendant Greenstreet's sales were also made pursuant to 10b5-1 trading plans, but she too entered into those plans while in possession of material adverse information about Patisiran. Specifically, Defendant Greenstreet's 2018 sales were made pursuant to a Rule 10b5-1

trading plan that she adopted on January 17, 2018 – when she was already aware of both the design flaws in APOLLO III for testing the safety and efficacy of Patisiran in cardiac manifestations of hATTR Amyloidosis, and the serious adverse cardiac death rates that resulted from the APOLLO III data. Accordingly, Defendant Greenstreet’s insider sales are highly probative of scienter.

236. In total, the pattern and suspicious timing and amounts of these Insider Defendants’ sales is unmistakable and highly probative of scienter.

2. Alnylam was Motivated to Sell Approximately 5.2 Million Shares of the Company’s Common Stock in the SPO

237. Alnylam and the other Individual Defendants were also highly motivated to sell 5.2 million shares of Alnylam common stock through a November 14, 2017 SPO, which was right on the heels of the Company’s final analysis of APOLLO III data. These shares, as well as the approximately 800,000 additional shares bought by the underwriters, yielded net proceeds for the Company of \$800 million. The Individual Defendants needed to ensure there was sufficient demand for these shares through their aggressive promotion of Patisiran and, accordingly, misled the market into believing Patisiran could treat a much larger patient population. Additionally, the Individual Defendants wanted to show that they could execute on the Alnylam 2020 plan to transform the Company from an R&D company to a commercialized company.

238. Alnylam offered the 5.2 million shares for sale in the SPO on November 14, 2017 – less than two weeks after announcing the Company’s final review of the APOLLO III data, which caused Alnylam stock to rise 10%. At the latest, by this final data review, the Individual Defendants knew that the 3.5 to 1 drug to placebo cardiac death ratio would imperil the study.

239. The Individual Defendants also personally sold \$21 million around the time of the SPO – during a three-week period between October 30, 2017 and November 22, 2017.

240. The Individual Defendants were also motivated to commit fraud to artificially inflate Alnylam's stock price and increase the proceeds from the SPO.

3. Alnylam Was in a Race Against Pfizer and Ionis to Bring the First FDA-Approved ATTR Amyloidosis Drug Treatment to Market

241. Defendants were also highly motivated to commit the fraud alleged herein because they were determined to beat Pfizer and Ionis and be the first to market a FDA-approved drug to treat hATTR Amyloidosis. After the failure of Revusiran, Defendants materially misrepresented APOLLO III, particularly as it related to cardiac patients, because they knew they had to convince the market that Patisiran was superior to similar pending drugs being developed by Alnylam's competitors, including Pfizer and Ionis. The race to capture the broadest patient population for hATTR Amyloidosis treatment was hotly contested, and would have a direct impact on the value of Alnylam stock (of which the Individual Defendants were large shareholders).

242. Ionis submitted its NDA to the FDA for its hATTR drug, Tegsedi, in November 2017 to treat polyneuropathy.

243. Alnylam submitted its NDA to the FDA for Patisiran in December 2017.

244. On March 29, 2018, Pfizer reported that its hATTR Amyloidosis drug, Tafamidis, which was intended to treat cardiomyopathy, succeeded in its Phase 3 trial, causing Alnylam stock to fall by over 25%, further underscoring the importance of the race to gain FDA approval for Patisiran.

245. Notably, Alnylam tried to downplay Pfizer's positive results, claiming, *inter alia*, that Patisiran was superior to Tafamidis, in relevant part, as follows:

Indirect Comparison Of Patisiran and Tafamidis For Treatment Of Hereditary
Transthyretin-Mediated (hATTR) Amyloidosis With Polyneuropathy

Patisiran

Evaluated in a randomized, placebo-controlled Phase 3 APOLLO study (NCT01960348) and showed significant improvement in primary endpoint Modified-Neuropathy Impairment Score +7 (mNIS+7) and secondary endpoint Norfolk Quality of Life (Norfolk QOL-DN) compared to placebo and was generally well tolerated.

Tafimidis

In the Phase 3 placebo-controlled study (Fx-005; NCT00409175), the co-primary endpoints of Neuropathy Impairment Score of the Lower Limbs (NIS-LL) response (<2 increase in NIS-LL) and Norfolk QOL-DN **were not statistically significantly different from placebo in the intention-to-treat (ITT) population at 18 months.**

<https://www.alnylam.com/wp-content/uploads/2018/07/5.-Coelho-ITC-Pati-v-Taf-PNS-2018.pdf>.

246. An April 2, 2018 *Biopharmadive* article discussed the ongoing race between Alnylam, Pfizer, and Ionis to gain FDA-approval for their respective hATTR Amyloidosis drug treatments, and shows that analysts thought Alnylam, driven in large part by the statements made by the Individual Defendants, was leading that race:

Alnylam's drug, called patisiran, is seen by many analysts as more potent and efficacious in easing the symptoms of the rare disease — which causes progressively more severe organ damage, leading to neuropathy and cardiomyopathy.

Ionis may win FDA approval for its rival candidate inotersen first, with a decision expected in early July. Alnylam won't be far behind and could potentially win an OK by August.

But Pfizer's results could complicate the competitive mix.

247. Pfizer submitted its NDA to the FDA for its ATTR drug Tafimidis in January 2019.

248. On May 6, 2019, Pfizer won FDA approval to treat hATTR-related cardiomyopathy with Tafimidis.

249. Convincing the market that Alnylam would be the first to bring a hATTR drug to market that could address polyneuropathy and cardiomyopathy was critical, and the Individual Defendants were highly motivated to commit fraud to do so.

4. Alnylam Had Serious Issues With Cardiac-Related Deaths in Drug Trials in the Past

250. As alleged above, Alnylam has had past issues with cardiac patients suffering cardio-related deaths while on its drugs. In the ENDEAVOUR trial, for example, Alnylam discontinued development of Revusiran after a 4:1 death imbalance in Revusiran-treated patients was witnessed as compared to those on placebo.

251. This is precisely what happened here too. Cardiac patients treated with Patisiran in APOLLO III died with a ratio of 3.5 to 1 compared to the placebo, which was very close to the 4:1 ratio that ended the Revusiran trial. Nomura analyst Christopher Marai, among others, noticed the issue:

A Platform Problem? Revusiran Cardiac Nightmares Revisited

Recall, ALNY terminated their Phase 3 ENDEAVOUR TTRsc revusiran program following findings of fatal cardiac sAE's (an imbalance in mortality on revusiran arm vs. placebo). The company investigated this imbalance and summarized the findings here (Fig. 1). We believe the FDA's cardiac concerns warrant additional scrutiny in light of ALNY's prior observations in this patient population with drugs of similar MOA. This may indicate general cardiac toxicities associated with the drug platform (leading to death or requirement of pacemakers; see above).

252. After their experience with the ENDEAVOUR trial, the Individual Defendants knew or recklessly disregarded that the safety data related to APOLLO III, particularly as it related to cardiac deaths, was of key importance, and that the FDA would have serious concerns with the cardiac deaths witnessed in APOLLO III.

253. The Individual Defendants knew about the serious safety concerns with cardiac death in APOLLO III at the latest in or around September 2017 when they first received the data

concerning APOLLO III. Safety data would have been the first metric reviewed by the Individual Defendants in light of Alnylam's prior history with safety issues in its studies.

5. Defendants Knew the FDA Would Not Approve Patisiran for Cardiac Patients or Include Cardiac Data on Patisiran's Label Because APOLLO III Did Not Test the Safety and Efficacy of the Drug on Cardiac Patients

254. Defendants knew it was impossible for the FDA to approve a drug without support for its efficacy. APOLLO III was not designed to test Patisiran's efficacy and safety for cardiac patients. *See* ¶¶41-44.

255. Alnylam is run by a team of highly educated pharmaceutical executives. In addition to their respective PhDs in molecular biology and molecular immunology, Defendants John Maraganore and Akshay Vaishnaw, Alnylam's CEO and President of R&D, respectively, have developed and commercialized several drugs at previous companies. Prior to joining Alnylam, Defendant Barry Greene, Alnylam's President, led the approval and launch of VELCADE (bortezomib) for Millenium Pharmaceuticals. Alnylam's COO, Defendant Yvonne Greenstreet, earned her medical degree from the University of Leeds, UK and an MBA degree from INSEAD, France. She previously served as the Senior Vice President and Head of Medicines Development at Pfizer.

256. As highly educated pharmaceutical executives, Defendants Greene, Maraganore, Greenstreet and Soni were well aware that it was impossible for the FDA to approve Patisiran without the requisite efficacy and safety data.

6. With the Cardiomyopathy Drug Revusiran Scuttled, Defendants Were Motivated to Push the Dual Labelling Narrative For Patisiran – And Supplement Projected Revusiran Earnings with Patisiran

257. Defendants were highly motivated to commit fraud to ensure success after the failure of the Revusiran trial, which erased over 50% of the value from Alnylam shares. Indeed,

Alnylam lost a critical revenue driver when the ENDEAVOUR trial for Revusiran was halted, causing Alnylam to be unable to market an RNAi drug to patients with hATTR Amyloidosis with cardiac manifestations. This substantial market was now unavailable to the Company.

258. Defendants were motivated to misrepresent Patisiran's likelihood of obtaining a broad label for the treatment of cardiac manifestations of hATTR Amyloidosis because the failure of the ENDEAVOUR trial had taken away any possibility of Defendants selling a drug to treat the substantially larger pool of patients.

7. Patisiran Was Part of Alnylam's "2020" Plan

259. Alnylam repeatedly stated that it "was focused on advancement of our Alnylam 2020 strategy for the development and commercialization of RNAi therapeutics as a potential new class of innovative medicines. Specifically, our goal is to achieve, by the end of 2020, a company profile with three marketed products and ten RNAi therapeutic clinical programs, including four in late stages of development, across our three STArs."

260. As a company transitioning from R&D to marketing new drugs, the Individual Defendants were motivated to commit fraud to ensure the success of Alnylam's 2020 plan.

8. Patisiran's Labelling was a Frequent Topic of Investor Focus and Analyst Questioning

261. The Individual Defendants were repeatedly asked specific questions from analysts about Patisiran's labelling and the robustness of APOLLO III. Analysts specifically focused in on whether or not the label could possibly include any labelling data. The Individual Defendants confidently responded to these questions by repeatedly affirming that Patisiran would receive a broad label with cardiac data. Thus, the Individual Defendants were well aware of the issues relating to Patisiran and APOLLO III.

LOSS CAUSATION/ECONOMIC LOSS

262. During the Class Period, as detailed herein, Alnylam securities were artificially inflated due to Defendants' materially false and misleading public statements. When Defendants' prior misrepresentations were disclosed and became apparent to the market, the price of Alnylam securities fell as the prior artificial inflation came out.

263. As a result of their purchases of Alnylam securities during the Class Period, Plaintiff and the Class suffered economic loss, *i.e.*, damages under the federal securities laws.

264. The decline in price of Alnylam securities after the corrective disclosures on August 10, 2018, and September 12, 2018, were the direct and proximate results of the Defendants' misrepresentations being revealed to investors and the market.

265. The decline in the price of Alnylam securities was also the direct and proximate result of the materialization of the concealed investment risks concerning Alnylam.

266. Defendants materially false and misleading statements relate to undisclosed risks concerning, *inter alia*: (i) the purported efficacy of Patisiran for the treatment of cardiac manifestations of hATTR Amyloidosis; (ii) the purported safety of Patisiran for the treatment of cardiac manifestations of hATTR Amyloidosis; (iii) the purported likelihood of obtaining FDA approval for a broad-based label for Patirisan that would include both polyneuropathy and cardiomyopathy manifestations of hATTR Amyloidosis; (iv) the purported likelihood of obtaining FDA approval for the inclusion of cardiac data from APOLLO III on the label for Patirisan; and (v) the purported design of APOLLO III to achieve the foregoing.

267. The first partial corrective disclosure occurred on August 10, 2018, when it was revealed that the FDA had only approved Patisiran for polyneuropathy, and did not approve Patisiran for cardiomyopathy treatment or allow any cardiac data from APOLLO III to be included

on the label for the drug. Notably, this partial corrective disclosure did not disclose to the market the FDA's reasoning for declining to include cardiomyopathy or cardiac data on Patisiran's label, and, at the time of this disclosure through September 12, 2018, Defendants continued to paint a rosy picture of the cardiac data from APOLLO III and about the future likelihood of the FDA broadening the label for Patisiran.

268. After the adverse August 10, 2018 announcement concerning Alnylam's failure to obtain a label that included, at a minimum, cardiac data, Alnylam stock dropped approximately 6% from \$97.38 per share to \$90.95 on August 13, 2018.

269. The second and final corrective disclosure occurred on September 12, 2018, when analysts disclosed that an FDA Report had recently revealed – in very strong language – the true extent of Alnylam's failure to obtain a broad-based label for Patisiran, which, at a minimum, included cardiac data from APOLLO III. Indeed, the FDA Report flatly stated that Alnylam “does not provide any efficacy data” as to cardiomyopathy. As such, Alnylam would need to back to the drawing board and complete a new study addressing Patisiran's efficacy for cardiac patients. The FDA Report also detailed at length the troubling back and forth between Alnylam and the FDA over the data underlying the 3.5 to 1 cardiac drug to placebo patient death ratio; namely, that Alnylam tried to re-categorize two placebo stroke deaths as cardiac-related to bring the ratio below 3.5 to 1 (*see* ¶70), and that the FDA had “serious” concerns with the cardiac safety profile of Patisiran.

270. Based on Defendants' statements, analysts expected Alnylam to get a label that – at a minimum – included cardiac data.

271. After the adverse September 12, 2018 reports revealing the full extent of the fraud perpetrated by Defendants, Alnylam stock fell approximately 5.5%, from \$99.11 per share to \$94.75.

272. The timing and magnitude of the price declines in Alnylam securities negate any inference that the loss suffered by Plaintiff and the other Class members was caused by changed market conditions, macroeconomic or industry factors or Company-specific facts unrelated to the Defendants' statements. The economic loss, *i.e.*, damages, suffered by Plaintiff and the other Class members was a direct result of Defendants' misstatements and omissions and the subsequent significant decline in the value of Alnylam securities when Defendants' misrepresentations were revealed.

CLASS ACTION ALLEGATIONS

273. Plaintiff brings this action as a class action pursuant to Federal Rule of Civil Procedure 23(a) and (b)(3) on behalf of a Class, consisting of all those who purchased or otherwise acquired Alnylam securities during the Class Period (the "Class") and were damaged upon the revelation of the alleged corrective disclosures. Excluded from the Class are Defendants herein, the officers and directors of the Company, at all relevant times, members of their immediate families and their legal representatives, heirs, successors, or assigns and any entity in which the Defendants have or had a controlling interest.

274. The members of the Class are so numerous that joinder of all members is impracticable. Throughout the Class Period, Alnylam securities were actively traded on the NASDAQ under the ticker symbol "ALNY". While the exact number of Class members is unknown to Plaintiff at this time and can be ascertained only through appropriate discovery, Plaintiff believes that there are hundreds or thousands of members in the proposed Class. Record

owners and other members of the Class may be identified from records maintained by Alnylam or its transfer agent and may be notified of the pendency of this action by mail, using the form of notice similar to that customarily used in securities class actions.

275. Plaintiff's claims are typical of the claims of the members of the Class as all members of the Class are similarly affected by Defendants' wrongful conduct in violation of federal law that is complained of herein.

276. Plaintiff will fairly and adequately protect the interests of the members of the Class and has retained counsel competent and experienced in class and securities litigation. Plaintiff has no interests antagonistic to or in conflict with those of the Class.

277. Common questions of law and fact exist as to all members of the Class and predominate over any questions solely affecting individual members of the Class. Among the questions of law and fact common to the Class are:

- a. whether the federal securities laws were violated by Defendants' acts as alleged herein;
- b. whether statements made by Defendants to the investing public during the Class Period misrepresented material facts about the business, operation and management of Alnylam;
- c. whether the Individual Defendants caused Alnylam to issue false and misleading statements during the Class Period;
- d. whether the Individual Defendants acted knowingly or recklessly in issuing false and misleading statements in violating the Exchange Act;
- e. whether the prices of Alnylam securities during the Class Period were artificially inflated because of the Defendants' conduct complained of herein; and

f. whether the members of the Class have sustained damages and, if so, what is the proper measure of damages.

278. A class action is superior to all other available methods for the fair and efficient adjudication of this controversy since joinder of all members is impracticable. Furthermore, as the damages suffered by individual Class members may be relatively small, the expense and burden of individual litigation make it impossible for members of the Class to individually redress the wrongs done to them. There will be no difficulty in the management of this action as a class action.

279. Plaintiff will rely, in part, upon the presumption of reliance established by the fraud-on-the-market doctrine in that:

280. Defendants made public misrepresentations or failed to disclose material facts during the Class Period;

281. the omissions and misrepresentations were material;

a. Alnylam securities are traded in an efficient market;

b. the Company's shares were liquid and traded with moderate to heavy volume during the Class Period;

c. the Company traded on the NASDAQ and was covered by multiple analysts;

d. the misrepresentations and omissions alleged would tend to induce a reasonable investor to misjudge the value of the Company's securities; and

e. Plaintiff and members of the Class purchased, acquired and/or sold Alnylam securities between the time the Defendants failed to disclose or misrepresented material facts and the time the true facts were disclosed, without knowledge of the omitted or misrepresented facts.

282. Based upon the foregoing, Plaintiff and the members of the Class are entitled to a presumption of reliance established by the Supreme Court in *Affiliated Ute Citizens of the State of Utah v. United States*, 406 U.S. 128, 92 S. Ct. 2430 (1972), as Defendants omitted material information in their Class Period statements in violation of a duty to disclose such information, as detailed above.

COUNT I

(Violations of Section 10(b) of the Exchange Act and Rule 10b-5 Promulgated Thereunder Against All Defendants)

283. Plaintiff repeats and realleges each and every allegation contained above as if fully set forth herein.

284. This Count is asserted against Defendants and is based upon Section 10(b) of the Exchange Act, 15 U.S.C. § 78j(b), and Rule 10b-5 promulgated thereunder by the SEC.

285. During the Class Period, Defendants engaged in a plan, scheme, conspiracy and course of conduct, pursuant to which they knowingly or recklessly engaged in acts, transactions, practices, and courses of business which operated as a fraud and deceit upon Plaintiff and the other members of the Class; made various untrue statements of material facts and omitted to state material facts necessary in order to make the statements made, in light of the circumstances under which they were made, not misleading; and employed devices, schemes and artifices to defraud in connection with purchase and sale of securities. Such scheme was intended to, and, throughout the Class Period, did: (i) deceive the investing public, including Plaintiff and other Class members, as alleged herein about APOLLO III and the efficacy and safety of Patisiran; (ii) artificially inflate and maintain the market price of Alnylam securities; and (iii) cause Plaintiff and other members of the Class to purchase or otherwise acquire Alnylam securities. In furtherance of this unlawful scheme, plan and course of conduct, Defendants, and each of them took the actions set forth herein.

286. Pursuant to the above plan, scheme, conspiracy and course of conduct, each of the Defendants participated directly or indirectly in the preparation and/or issuance of the quarterly and annual reports, SEC filings, press releases and other statements and documents described above, including statements made to securities analysts and the media that were designed to influence the market for Alnylam securities. Such reports, filings, releases, and statements were materially false and misleading in that they failed to disclose material adverse information and misrepresented the truth about APOLLO III and Patisiran's efficacy and safety.

287. By virtue of their positions at Alnylam, Defendants had actual knowledge of materially false and misleading statements and material omissions alleged herein and intended thereby to deceive Plaintiff and the other members of the Class, or, in the alternative, Defendants acted with reckless disregard for the truth in that they failed or refused to ascertain and disclose such facts as would reveal the materially false and misleading nature of the statements made, although such facts were readily available to Defendants. Said acts and omissions of Defendants were committed willfully or with reckless disregard for the truth. In addition, each Defendant knew or recklessly disregarded that material facts were being misrepresented or omitted as described above.

288. Defendants' scienter is also supported by, inter alia, the Individual Defendants' insider stock sales, the November 2017 SPO, the motive to win the race to be the first company to bring an hATTR drug to market, and Alnylam's past problem with cardiac deaths in the ENDEAVOUR trial. *See* ¶¶ 220-258.

289. Information showing that Defendants acted knowingly or with reckless disregard for the truth is within Defendants' knowledge and control. As the senior managers of Alnylam, the Individual Defendants had knowledge of the details of Alnylam internal affairs. As highly

educated pharmaceutical executives who are well acquainted with drug trials, the Individual Defendants also knew it was impossible for the FDA to approve a broad label for Patisiran or include cardiac-related data on the drug's label for the reasons discussed *supra*.

290. The Individual Defendants are liable both directly and indirectly for the wrongs complained of herein. Because of their positions of control and authority, the Individual Defendants were able to and did, directly or indirectly, control the content of the statements of Alnylam. As officers and/or directors of a publicly-held company, the Individual Defendants had a duty to disseminate timely, accurate, and truthful information with respect to Alnylam's business, operations, future financial condition and future prospects. As a result of the dissemination of the aforementioned false and misleading reports, releases and public statements, the market price for Alnylam securities was artificially inflated throughout the Class Period. In ignorance of the adverse facts concerning Alnylam business which were concealed by Defendants, Plaintiff and the other members of the Class purchased or otherwise acquired Alnylam securities at artificially inflated prices and relied upon the price of the securities, the integrity of the market for the securities and/or upon statements disseminated by Defendants, and were damaged thereby.

291. During the Class Period, Alnylam securities were traded on an active and efficient market. Plaintiff and the other members of the Class, relying on the materially false and misleading statements described herein, which the Defendants made, issued or caused to be disseminated, or relying upon the integrity of the market, purchased or otherwise acquired shares of Alnylam securities at prices artificially inflated by Defendants' wrongful conduct. Had Plaintiff and other members of the Class known the truth, they would not have purchased or otherwise acquired said securities, or would not have purchased or otherwise acquired them at the inflated prices that were paid. At the time of the purchases and/or acquisitions by Plaintiff and the Class, the true value of

Alnylam securities was substantially lower than the prices paid by Plaintiff and the other members of the Class. The market price of Alnylam securities declined sharply upon the two public disclosures of the facts alleged herein to the injury of Plaintiff and Class members.

292. By reason of the conduct alleged herein, Defendants knowingly or recklessly, directly or indirectly, have violated Section 10(b) of the Exchange Act and Rule 10b-5 promulgated thereunder.

293. As a direct and proximate result of Defendants' wrongful conduct, Plaintiff and the other members of the Class suffered damages in connection with their respective purchases, acquisitions, and sales, of the Company's securities during the Class Period, upon the disclosure that Defendants had been making misrepresentations to the investing public.

COUNT II

(Violations of Section 20(a) of the Exchange Act Against The Individual Defendants)

294. Plaintiff repeats and realleges each and every allegation contained in the foregoing paragraphs as if fully set forth herein.

295. During the Class Period, the Individual Defendants participated in the operation and management of Alnylam, and conducted and participated, directly and indirectly, in the conduct of Alnylam business affairs. Because of their senior positions, as well as highly educated pharmaceutical executives with experience running drug trials, they knew the adverse non-public information about APOLLO III and Patisiran.

296. As officers and/or directors of a publicly owned company, the Individual Defendants had a duty to disseminate accurate and truthful information with respect to APOLLO III and Patisiran, as detailed *supra*, and to correct promptly any public statements issued by Alnylam which had become materially false or misleading.

297. Because of their positions of control and authority as senior officers, the Individual Defendants were able to, and did, control the contents of the various reports, press releases, conference calls, and public filings which Alnylam disseminated in the marketplace during the Class Period concerning Alnylam results of operations. Throughout the Class Period, the Individual Defendants exercised their power and authority to cause Alnylam to engage in the wrongful acts complained of herein. The Individual Defendants therefore, were “controlling persons” of Alnylam within the meaning of Section 20(a) of the Exchange Act.

298. Each of the Individual Defendants, therefore, acted as a controlling person of Alnylam. By reason of their senior management positions and/or being directors of Alnylam, each of the Individual Defendants had the power to direct the actions of, and exercised the same to cause, Alnylam to engage in the unlawful acts and conduct complained of herein. The Individual Defendants therefore, were “controlling persons” of Alnylam within the meaning of Section 20(a) of the Exchange Act. In this capacity, they participated in the unlawful conduct alleged which artificially inflated the market price of Alnylam securities.

299. By reason of the above conduct, the Individual Defendants are liable pursuant to Section 20(a) of the Exchange Act for the violations committed by Alnylam.

PRAYER FOR RELIEF

WHEREFORE, Plaintiff prays for relief and judgment as follows:

- (a) Determining that this action is a proper class action and certifying Plaintiff as class representative under Rule 23 of the Federal Rules of Civil Procedure;
- (b) Awarding damages in favor of Plaintiff and the other Class members against all Defendants, jointly and severally, for all damages sustained as a result of Defendants’

- violations of the Securities Exchange Act of 1934, in an amount to be proven at trial, including interest thereon;
- (c) Awarding Plaintiff and the Class their reasonable costs and expenses incurred in this action including counsel fees and expert fees; and
- (d) Awarding such other and further relief as the Court may deem just and proper.

DEMAND FOR TRIAL BY JURY

Plaintiff hereby demands a trial by jury.

DATED: July 3, 2019

Respectfully submitted,

BERMAN TABACCO

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Lead Counsel for Lead Plaintiff

CERTIFICATE OF SERVICE

I hereby certify that on July 3, 2019, a true and correct copy of the foregoing document was served electronically through the ECF system on all counsel of record.

/s/ Leslie R. Stern
Leslie R. Stern